

Gary West, Darryl Heard, & Nigel Caulkett

Zoo Animal & Wildlife Immobilization and Anesthesia







ZOO ANIMAL AND WILDLIFE IMMOBILIZATION AND ANESTHESIA

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Gary West, DVM, Dipl ACZM

Oklahoma City Zoo and Botanical Garden Oklahoma State University's College of Veterinary Medicine

Darryl Heard, BSc, BVMS, PhD, Dipl ACZM University of Florida College of Veterinary Medicine

Nigel Caulkett, DVM, MVetSc, Dipl ACVA University of Calgary College of Veterinary Medicine



Gary West, DVM, Dipl ACZM is the Director of Veterinary Services at the Oklahoma City Zoo and an Adjunct Assistant Professor at Oklahoma State University.

Darryl Heard, BSc, BVMS, PhD, Dipl ACZM is an Associate Professor and Service Chief of Zoological Medicine at the University of Florida.

Nigel Caulkett, DVM, MVetSc, Dipl ACVA is a Professor of Anesthesiology at the University of Calgary.

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Contributors

Noha Abou-Madi, DVM, MSc, Dipl ACZM

Section of Wildlife Health Department of Clinical Sciences College of Veterinary Medicine Cornell University Ithaca, New York 14853-6401 Phone: 607-253-3371

Fax: 607-253-3271

E-mail: gvk2@cornell.edu;na24@cornell.edu

Fred Antonio

General Curator Central Florida Zoological Park P.O. Box 470309 Lake Monroe, Florida 32747-0309 Phone: 407-323-4450 ext 140

Fax: 407-321-0900

E-mail: freda@centralfloridazoo.org

Jon M. Arnemo, DVM, PhD

Professor and Wildlife Veterinarian Section of Arctic Veterinary Medicine Department of Food Safety and Infection Biology Norwegian School of Veterinary Science Tromsø, Norway

James Bailey, DVM, MS, Dipl ACVA

University of Florida
College of Veterinary Medicine
Service Chief
Anesthesia and Pain Management
P.O. Box 100136
Gainesville, Florida 32610-0136

Phone: 352-258-6600

E-mail: baileyj@mail.vetmed.ufl.edu

Ray L. Ball, DVM, MRCVS

Associate Veterinarian Busch Gardens Tampa Bay 3605 Bougainvillea Avenue Tampa, Florida 33612 Phone: 813-987-5562 Fax: 813-987-5548

E-mail: Dr.Ray.Ball@BuschGardens.com

Mads F. Bertelsen, DVM, DVSc

Staff Veterinarian Centre for Zoo and Wild Animal Health Copenhagen Zoo Roskildevej 38 DK-2000 Frederiksberg, Denmark Phone/office: +45-72200227 Phone/cell: +45-30167327 E-mail: mfb@zoo.dk

Kate Bodley

Veterinarian, Melbourne Zoo P.O. Box 74 Parkville Victoria 3052, Australia Phone: +61 3-9285-9431 Fax: +61 3-9285-9349 E-mail: kbodley@zoo.org.au

David B. Brunson, DVM, MS, Dipl ACVA

Veterinary Specialty Team, Pfizer Animal Health 2780 Waubesa Avenue Madison, Wisconsin 53711

Mitchell Bush, DVM, Dipl ACZM

Senior Veterinarian Conservation and Research Center Smithsonian's National Zoo 1500 Remount Road Front Royal, Virginia 22630 Phone: 540-635-6551 Fax: 540-635-6551 E-mail: mbush@si.edu

Tracy Carer, BS, MS, PhD

Adjunct Professor Oklahoma State University Department of Zoology 415 LSW Stillwater, Oklahoma 74078 Phone: 405-744-9675 Fax: 405-744-7824 E-mail: tracy.carter@okstate.edu

Nigel. A Caulkett, DVM, MVetSc, Dipl ACVA

Professor of Anaesthesiology University of Calgary Faculty of Veterinary Medicine 3330 Hospital Drive NW Calgary, Alberta, Canada T2N 4N1

Elizabeth Chittick, DVM, Dipl ACZM

Disney's Animal Programs 1200 Savannah Circle East Bay Lake, Florida 32830

E-mail: Elizabeth.J.Chittick@disney.com

Scott B. Citino, DVM, Dipl ACZM

White Oak Conservation Center 581705 White Oak Road Yulee, Florida 32097 Phone: 904-225-3387

Fax: 904-225-3337

E-mail: scottC@wogilman.com

Thomas G. Curro, DVM, MS

Staff Veterinarian

Six Flags Great Adventure Wild Safari

Highway 537

Jackson, New Jersey 08527 Phone: 732-928-2000 ext. 2077 E-mail: tcurro@sftp.com

Chris Dold

SeaWorld of Florida Veterinary Services Department 7007 SeaWorld Drive Orlando, Florida 32821

Gregory J. Fleming, DVM, Dipl ACZM

Veterinarian, Disney's Animal Programs Disney's Animal Kingdom, Animal Programs Administration Building Veterinary Services

1200 Savannah Circle, East Bay Lake, Florida 32830 Phone: 407-938-1925 Fax: 407-938-3266

E-mail: greg.fleming@disney.com

Kurt Grimm, DVM, MS, PhD, Dipl ACVA and ACVCP

Veterinary Specialist Services PC

P.O. Box 504

Conifer, Colorado 80433 Phone: 303-918-1321 Fax: 303-816-4404

E-mail: anesthesiologist@veterinaryspecialistservices.com

Cornelia (Conny) Gunkel, Dr MedVet, Dipl ACVA

Assistant Professor of Anesthesiology

Oregon State University College of Veterinary Medicine

219 Magruder Street Corvallis, OR 97331 Phone: 541-737-6859

Fax: 541-737-6879

E-mail: conny.gunkel@oregonstate.edu

Nina Hahn, DVM, PhD, Dipl ACLAM

Associate Director

Office of Laboratory Animal Care Northwest Animal Facility, Room 203 University of California Berkeley Berkeley, California 94720-7150

Phone: 510-643-9667 Fax: 510-643-9929

E-mail: nhahn@olac.berkeley.edu

Sonia Hernandez-Divers, DVM, Dipl ACZM

PhD Candidate and Adjunct Assistant Professor Institute of Ecology and College of Veterinary Medicine

University of Georgia Athens, Georgia 30605 Phone: 706-542-2968 E-mail: shernz@aol.com

Jerry C. Haigh, BVMS, MSc, FRCVS, Dipl ACZM

Professor, Dept of Large Animal Clinical Sciences

University of Saskatchewan

52 Campus Drive

Saskatoon, Saskatchewan, Canada S7N 5B4

Martin Haulena, DVM, MSc

Staff Veterinarian Vancouver Aquarium P.O. Box 3232

Vancouver, British Columbia, Canada V6B 3X8

Phone: 604-659-3468 Fax: 604-659-3469

E-mail: Martin.Haulena@vanaqua.org

Michelle G. Hawkins, DVM, Dipl ABVP

Assistant Professor, Companion Exotic Animal

Medicine and Surgery

Department of Medicine and Epidemiology

School of Veterinary Medicine University of California, Davis Davis, California 95616 Phone: 530-752-1393

Fax: 530-752-0414

E-mail: mghawkins@ucdavis.edu

Darryl J. Heard BSc, BVMS, PhD, Dipl ACZM

Associate Professor Zoological Medicine Department of Small Animal Clinical Sciences

College of Veterinary Medicine

University of Florida

Gainesville, Florida 32610-0126 Phone: 352-392-4700 ext. 4708

Fax: 352-392-6125

E-mail: heardd@mail.vetmed.ufl.edu

Bruce Heath, DVM, MS, Dipl ACVA

Seven Seven Anesthesia/Consulting

4290 Crest Road

Fort Collins, Colorado 80526-4006

Peter Holz, BVSc, DVSc, MACUSc, Dipl ACZM

Associate Veterinarian Healesville Sanctuary

P.O. Box 248

Healesville, Victoria 3777

Australia

Phone: 613-5957-2864 Fax: 613-5957-2860 E-mail: pholz@zoo.org.au

William H. Horne, DVM, PhD, Dipl ACVA

Professor, Section of Anesthesia and Pain Medicine

Department of Clinical Sciences

Cornell University College of Veterinary Medicine

Ithaca, New York 14853 Phone: 607-253-4145 Fax: 607-253-3497

E-mail: wah27@cornell.edu

Ramiro Isaza, MSc, DVM, Dipl ACZM

Associate Professor Zoological Medicine Department of Small Animal Clinical Sciences

College of Veterinary Medicine

University of Florida

Gainesville, Florida 32610-0126 Phone: 352-392-4700 ext. 5743 E-mail: isazar@mail.vetmed.ufl.edu

Randall Junge, MS, DVM, Dipl ACZM

Director of Animal Health

St. Louis Zoo

1 Government Drive

Saint Louis, Missouri 63110 Phone: 314-781-0900 ext. 487

Fax: 314-647-7969 E-mail: junge@stlzoo.org

Jeff Ko, DVM, MS, Dipl ACVA

Professor Veterinary Anesthesia Department of Clinical Sciences School of Veterinary Medicine

Purdue University

625 Harrison Street, West Lafayette, Indiana 47907-2026

Phone: 765-496-2026 Fax: 3756-496-1108 E-mail: jcko@purdue.edu

George V. Kollias, DVM, PhD, Dipl ACZM

J. Hyman Professor of Wildlife Medicine

College of Veterinary Medicine

Cornell University Ithaca, New York 14853 Phone: 607-253-3049 Fax: 607-253-3271

E-mail: gvk2@cornell.edu

Maud Lafortune, DMV, MSc, Dipl ACZM

Associate Veterinarian Houston Zoo, Inc. 1513 North MacGregor Drive Houston, Texas 77030

Phone: 713-533-6706

E-mail: mlafortune@houstonzoo.org

Leigh A. Lamont, DVM, MS, Dipl ACVA

Assistant Professor of Anesthesiology Department of Companion Animals Atlantic Veterinary College 550 University Avenue Charlottetown, Prince Edward Island Canada C1A 4P3

Fax: 902-628-4316 E-mail: llamont@upei.ca

Jennifer N. Langan, DVM, Dipl ACZM

Clinical Assistant Professor Zoological Medicine

University of Illinois

College of Veterinary Medicine Associate Zoo Veterinarian

Brookfield Zoo 3300 Golf Road

Brookfield, Illinois 60513 Phone: 708-485-0263 ext. 596

Fax: 708-485-0269

E-mail: jelangan@brookfieldzoo.org

R. Scott Larsen, DVM, MS, Dipl ACZM

Assistant Professor of Captive and Free-ranging Wildlife University of California, Davis

Veterinary Medical Teaching Hospital

One Shields Avenue Davis, California 95616 Phone: 530-752-2985 Fax: 530-752-3318

E-mail: slarsen@ucdavis.edu

Gregory A. Lewbart, MS, VMD, Dipl ACZM

Professor of Aquatic Animal Medicine North Carolina State University College of Veterinary Medicine 4700 Hillsborough Street Raleigh, North Carolina 27606

Phone: 919-513-6439 Fax: 919-513-6336

E-mail: greg_lewbart@ncsu.edu

Michael Loomis, DVM, Dipl ACZM

Chief Veterinarian

North Carolina Zoological Park

4401 Zoo Parkway

Asheboro, North Carolina 27205

Phone: 336-879-2891 Fax: 336-879-7631

E-mail: mike.loomis@ncmail.net

Michael Lynch

Veterinarian, Melbourne Zoo

P.O. Box 74

Parkville, Victoria 3052 Australia

Phone: +61 3-9285-9431 Fax: +61 3-9285-9349 E-mail: mlynch@zoo.org.au

Karen Machin, DVM, MSc, PhD

Associate Professor Department of Biomedical Sciences University of Saskatchewan 52 Campus Drive Saskatoon, Saskatchewan, Canada S7N 5B4

Khursheed Mama, BVSC, DVM, Dipl ACVA

Associate Professor

Department of Clinical Sciences Colorado State University

Fort Collins, Colorado 80523 Phone: 970-297-4124

Fax: 970-297-1275

E-mail: kmama@colostate.edu

Michele Miller, DVM, PhD

Veterinary Services Operation Manager Disney's Animal Kingdom 1200 North Savannah Circle East Bay Lake, Florida 32830

Phone: 407-939-7316 Fax: 407-939-6240

E-mail: michele.miller@disney.com

Anneke Moresco, DVM, MS, PhD Candidate

University of California, Davis

Department of Veterinary Pathology, Microbiology, and

Immunology 1126 Haring Hall One Shields Avenue Davis, California 95616 Phone: 530-754-7963 Fax: 530-752-3349

E-mail: amoresco@ucdavis.edu

Pete vdB Morkel, BVSc

Rhino Coordinator Frankfurt Zoological Society Ngorongoro Conservation Area P.O. Box 1

Ngorongoro, Tanzania Phone: 255-27-2537134 E-mail: petemorkel@fzs.org

Craig Mosley, DVM, MSc, Dipl ACVA

Assistant Professor of Anesthesiology Oregon State University 229 Magruder Corvallis, OR 97331

Daniel M. Mulcahy, PhD, DVM, Dipl ACZM

Wildlife Veterinarian U.S. Geological Survey Alaska Science Center 1011 East Tudor Road Anchorage, Alaska 99503 Phone: 907-786-3451

Fax: 907-786-3636

E-mail: daniel_mulcahy@usgs.gov

Donald L. Neiffer, VMD, Dipl ACZM

Veterinary Operations Manager Disney's Animal Programs

P.O. Box 10,000

Lake Buena Vista, Florida 32830

Phone: 407-938-2719 Fax: 407-939-6391

Rolf-Arne Ølberg, DVM, DVSc

Director of Animal Care Kristiansand Dyrepark 4609 Kardemomme By

Norway

Phone: +47 97059860 Fax: +47 38043367

E-mail: rolfarne@dyreparken.no

Luis R. Padilla, DVM

Veterinary Medical Officer Smithsonian National Zoological Park 3001 Connecticut Avenue NW Washington, D.C. 20008 Phone: 202-633-2747

Fax: 202-673-4733 E-mail: padillal@si.edu

John M. Parker, DVM

Campus Veterinarian
Office of Laboratory Animal Care
Northwest Animal Facility, Room 203
University of California Berkeley
Berkeley, California 94720-7150
Phone: 510-672-0044

Fax: 510-643-9929

E-mail: jparker@olac.berkeley.edu

Peter J. Pascoe, BVSc, Dipl ACVA

Professor of Veterinary Anesthesiology and Critical Patient Care

Department of Surgical and Radiological Sciences
School of Veterinary Medicine

School of Veterinary Medicine University of California, Davis Davis, California 95616

Phone: 530-752-3151 Fax: 530-752-6042

E-mail: pjpascoe@ucdavis.edu

Jessica M. Paterson, DVM, MVetSc

Associate Professor of Anaesthesiology Department of Small Animal Clinical Sciences University of Saskatchewan 52 Campus Drive Saskatoon, Saskatchewan, Canada S7N 5B4

Robin W. Radcliffe, DVM, Dipl ACZM

Rhinoceros Conservation Medicine Program International Rhino Foundation/Cornell University 525 Spencer Road

S25 Spencer Road Ithaca, New York 14850 Phone: 607-253-4314 Fax: 607-253-3271

E-mail: RobinR@fossilrim.org

Sam Ridgway, DVM, PhD, Dipl ACZM

UCSD Veterinary Services SSC SD 235 PLBS 53560 Hull Street San Diego, California 92152-5001

Phone: 619-553-1374 Fax: 619-553-1346

E-mail: sridgway@UCSD.edu

Juergen Schumacher, DrMedVet, Dipl ACZM

Associate Professor of Avian and Zoological Medicine Service Chief, Avian and Zoological Medicine Department of Small Animal Clinical Sciences College of Veterinary Medicine The University of Tennessee

Knoxville, Tennessee 37996 Phone: 865-755-8221 Fax: 865-974-5554

E-mail: jschumacher@utk.edu

Jim Shaw, BS, MS, PhD

Professor, Oklahoma State University Department of Natural Resources, Ecology and Management 008 Ag Hall Stillwater, Oklahoma 74078 Phone: 405-744-9842

E-mail: jim.shaw@okstate.edu

Todd Shury, DVM

Fax: 405-744-3530

Wildlife Health Specialist, Parks Canada Department of Veterinary Pathology University of Saskatchewan Western College of Veterinary Medicine 52 Campus Drive Saskatoon, Saskatchewan, Canada S7N 5B4

Jessica Siegal-Willott, DVM

Resident, Zoological Medicine White Oak Conservation Center 581705 White Oak Road, ASB Yulee, Florida 32097

Phone/office: 904-225-3319 Phone/home: 904-225-3371 Phone/cell: 352-328-6288

Jonathan Sleeman, MA, VetMB, MRCVS, **Dipl ACZM**

Wildlife Veterinarian Commonwealth of Virginia Department of Game and Inland Fisheries 4010 West Broad Street Richmond, Virginia 23230 Phone: 804-367-9492 Fax: 804-367-9495 E-mail: jonathan.sleeman@dgif.virginia.gov

M. Andrew Stamper, DVM, Dipl ACZM

Research Biologist/Clinical Veterinarian The Seas, Disney's Animal Programs Walt Disney World Resorts EC Trl. W-251 2020 North Avenue of the Stars Lake Buena Vista, Florida 32830-1000 Phone: 407-560-5576 Fax: 407-560-5750

Mark D. Stetter, DVM, Dipl ACZM

Veterinary Services Director Disney's Animal Programs

1200 Savannah Circle East Bay Lake, Florida 32830 E-mail: Mark.stetter@disney.com

Gregory Timmel, DVM, MS

Campus Veterinarian Office of Laboratory Animal Care Northwest Animal Facility, Room 203 University of California Berkeley Berkeley, California 94720-7150 Phone: 510-643-9568

Fax: 510-643-0886

E-mail: gtimmel@olac.berkeley.edu

Kent A. Vliet, PhD

Senior Associate in Zoology Coordinator of Biological Sciences University of Florida Department of Zoology P.O. Box 118525 210 Carr Hall Gainesville, Florida 32611-8525

Phone: 352-392-1565 Fax: 352-392-4738

E-mail: kent.vliet@zoo.ufl.edu

Michael Walsh, BA, DVM

SeaWorld Orlando 7007 SeaWorld Drive Orlando, Florida 32821 Phone: 407-363-2366 Fax: 407-363-2377

Christian Walzer, Dr MedVet, Univ Prof

Zoo and Wildlife Veterinarian Research Institute of Wildlife Ecology University of Veterinary Medicine Savoyenstrasse 1, A-1160 Vienna, Austria

Phone: +43 14890915180 Fax: +43 14890915333 E-mail: chwalzer@eunet.at

Mary L. Weldele, BA

Associate Research Specialist Department of Psychology 3210 Tolman Hall #1650 University of California Berkeley Berkeley, California 94720-1650 Phone: 510-643-5154

Fax: 510-642-8321

E-mail: mweldele@berkeley.edu

Gary West, DVM, Dipl ACZM

Adjunct Assistant Professor Department of Clinical Sciences Oklahoma State University College of Veterinary Medicine Director Veterinary Services Oklahoma City Zoo and Botanical Garden 2101 NE 50th Street Oklahoma City, Oklahoma 73111

xii CONTRIBUTORS

Phone: 405-425-0249 Fax: 405-425-0220

E-mail: gwest@okczoo.com

Cathy Williams, DVM

Senior Veterinarian Duke University Primate Center 3705 Erwin Road

Durham, North Carolina 27705 Phone: 919-489-3364 ext. 221 Fax: 919-490-5394 E-mail: cwdvm@duke.edu

Murray R Woodbury, DVM, MSc

Associate Professor Department of Large Animal Clinical Sciences University of Saskatchewan 52 Campus Drive Saskatoon, Saskatchewan, Canada S7N 5B4

Preface

Anesthesia of zoo and wildlife species has improved rapidly over the last decade with new drugs, portable monitoring equipment, and methods of drug delivery. As certain species face a tenuous future in the wild and zoo animals become increasingly more popular, there is a huge responsibility when anesthetizing them.

With any textbook there will be omissions. There will also be immobilization protocols preferred by individuals that differ from those presented here. We have done our best, however, to include authors with experience immobilizing and anesthetizing the species they

cover. The reader will find the chapters well referenced, providing much more information for those who wish to delve deeper.

The goal of this book is to provide a comprehensive resource for anesthetizing any non-human animal. We hope it will be valuable for veterinary students, technicians, and clinicians, as well as biologists, wildlife managers, and researchers. We realize there is a paucity of information about analgesia in many species, and we encourage further study.

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Section I Pharmacology and Drug Delivery

1

Clinical Pharmacology

Kurt A. Grimm and Leigh A. Lamont

INTRODUCTION

Pharmacology is the study of drugs and their interactions with organisms (Page, 2002). Pharmacology incorporates aspects of statistics, biochemistry, biology, pathology, and medicine. Failure to interpret the description of drugs' pharmacological properties in the context of the clinical picture (i.e., clinical pharmacology) can result in unintended outcomes.

The pharmacological data available for most drugs are mean values derived from a relatively small number of individuals (usually healthy individuals). Although this approach provides a starting point for clinical use of drugs, individual responses can vary greatly because of disease states, body condition, environment, genetics, co-administered drugs, and many other factors. When the toxic dose is close to the therapeutic dose (as is often the case with drugs used for immobilization and anesthesia), careful titration of dose and patient monitoring are required. However, the nature of working with wildlife and captive non-domestic species often precludes baseline health assessment, individualization of dosing, and intensive patient monitoring. This is one factor associated with increased risk of adverse outcomes when capturing or anesthetizing non-domestic species. It should be appreciated also that advances in drug safety will likely result in only limited improvement in the safety of anesthesia and immobilization. Management of other risk factors through airway management, reduction of stress, and improvements in supportive care will be beneficial also.

PHARMACOKINETICS

Pharmacokinetics (PK) can be defined generally as what an organism does to a drug. Absorption, distribution, biotransformation, and elimination are processes that determine the concentration of drug at the site of action (i.e., biophase). Pharmacokinetic parameters are esti-

mates of these processes in the group of animals studied. These estimates can be used to predict or understand the way a drug interacts with an organism. It is important to understand that pharmacokinetic parameters can vary among individual animals and can be influenced by many different drug- and organism-related factors. Additionally, pharmacokinetic parameters are derived using mathematical models selected by the investigator. Usually there is no correlation between model components and anatomical structures.

PHARMACODYNAMICS

Pharmacodynamics (PD) can be defined generally as what a drug does to an organism. Pharmacodynamics includes intended drug effects as well as adverse drug actions. Drugs such as opioids, α_2 -adrenergic agonists, and antimuscarinics act by binding to relatively wellcharacterized receptor complexes located on cellular membranes. Non-steroidal antiinflammatory drugs (NSAIDs) inhibit prostaglandin production by binding to cyclooxygenase enzyme isoforms. Relating plasma drug concentrations to observed NSAIDs actions can be complex in comparison with other drugs (e.g., opioids) because of the different nature of the action. Preexisting prostaglandins, as well as the slower process of inhibiting an enzyme system, confound the relationship between drug concentration and effect. The molecular actions of inhalant anesthetics have not been completely characterized, even though their clinical use has been well described (Steffey, 2006).

Pharmacodynamic effects are predictable for most clinically used drugs; however, individual animal responses can vary considerably. Additionally, the nature of capture of free-ranging and captive wildlife often makes accurate dosing and drug delivery difficult or impossible. Therefore, close monitoring of patient response and preparation for supportive care are paramount to safe immobilization and anesthesia.

INHALANT ANESTHETICS

Inhalant anesthetics are commonly used in companion animal veterinary practice. Their use under field conditions is limited because of the requirement for specialized delivery devices and a supply of delivery gas (e.g., oxygen). However, inhalant anesthetics are used commonly in controlled settings such as zoological parks and research laboratories because of the ease of titration of anesthetic depth and rapidity of recovery. Inhalant anesthetics should be delivered by a well-maintained anesthetic machine and properly trained individuals. Although inhalant anesthetics are relatively safe, their low therapeutic index mandates frequent and careful monitoring of anesthetic depth.

Physics of Gases and Vapors

An understanding of the processes that influence the uptake and delivery of inhalant anesthetics allows the anesthetist to predict and respond to individual circumstances.

Brief Review of Molecular Theory Molecules in a liquid state have more vibrational energy than when in a solid state, and each molecule can move through the liquid. If heat is added to a liquid, each molecule gains more kinetic energy and eventually some overcome the forces exerted by their neighbors and are able to escape into the space above the liquid. This state is that of a gas or vapor. A gas is a phase of matter that expands indefinitely to fill a containment vessel. A vapor is the gaseous state of a material below its boiling point.

A vapor is in equilibrium with the liquid beneath it. Because both gaseous and liquid molecules have kinetic energy, they are in constant motion. The molecules in the vapor phase are striking the liquid–gas interface and returning to the liquid while liquid molecules are leaving the interface to become vapor. The relationship between these two phases depends mainly on the physicochemical properties of the molecules and the temperature of the system.

Vapor Pressure Molecules in a gaseous state possess kinetic energy and collide with the walls of the containment vessel. These collisions produce a force on the walls. This force is spread over a surface area and therefore is a pressure (Pressure = Force/Area). This pressure is called the vapor pressure. Because kinetic energy increases directly with temperature, vapor pressure always must be given with reference to the temperature at which it was measured (e.g., vapor pressure of water is 47 mmHg at 37°C).

When many gases are present in a mixture, such as with atmospheric air or during delivery of inhalant anesthetics, each gas has a vapor pressure that is independent of the other gases (Dalton's Law of Partial Pressures). It is convention to refer to vapor pressure as

partial pressure under these conditions. Partial pressure of an anesthetic agent is analogous to the concept of "free drug" and is important for determining the effect of the anesthetic (e.g., the level of central nervous system [CNS] depression correlates directly with the partial pressure of isoflurane within the brain) (see Table 1.1) (Steffey, 1996).

Vapor Concentration Vapor (i.e., partial) pressure is important for the observed pharmacological effect of inhalant anesthetics. However, almost all anesthesiologists refer to the amount of anesthetic delivered in units of volumes% (said as volumes-percent), or just %, which is a concentration. The fundamental difference between anesthetic partial pressure and anesthetic concentration is partial pressure relates to the absolute number of molecules and their kinetic energy, whereas concentration refers to the number of molecules of anesthetic relative to the total number of molecules present.

Critical Temperature The critical temperature is the temperature above which a substance cannot be liquefied no matter how much pressure is applied. The critical temperature of nitrous oxide is 36.5°C. Consequently, nitrous oxide can be (and is) a liquid below this temperature, but is a gas at greater temperatures. Placing a nitrous oxide tank near a heat source will produce volatilization of liquid nitrous oxide, resulting in a high tank pressure and danger of explosion or tank venting.

The critical temperature of oxygen is -119° C. Therefore, at room temperature oxygen cannot be liquefied. All compressed cylinders of medical oxygen contain only gas. There are liquid oxygen tanks, but the internal tank temperature is below -119° C.

Henry's Law Henry's law states that the solubility of a gas in a liquid is proportional to the pressure of the gas over the solution. It describes the solubility of an anesthetic in body fluids or other liquids. From it you can derive the following formula: $c = k \cdot P$; where c is the molar concentration (mol/L) of the dissolved gas and P is the pressure (in atmospheres) of the gas over the solution. For a given gas k is the Henry's Law constant and is dependent on temperature.

Table 1.1. Anesthetic agent vapor pressures at 20 and 24°C.

Anesthetic Agent	Vapor Pressure at 20°C in mmHg	Vapor Pressure at 24°C in mmHg
Methoxyflurane	23	28
Sevoflurane	160	
Enflurane	172	207
Isoflurane	240	286
Halothane	243	288
Nitrous oxide	Gas	Gas

Adapted from: Steffey EP. Inhalation anesthetics. In: Thurmon JT, Tranquilli WJ, Benson GJ, eds. *Lumb and Jones' Veterinary Anesthesia*, 3rd ed. Baltimore: Williams & Wilkins, 1996.

Partition Coefficient A partition coefficient is the ratio of the concentration of a substance in one medium relative to another at equilibrium. It is related to the solubility of an agent. At equilibrium the partial pressure is the same throughout the body, including the alveolar gas, but the concentration of total drug may be very different because of partitioning into tissues or body fluids (Table 1.2) (Steffey, 1996). Partition coefficients are not absolute constants for an anesthetic agent. Tissue composition may change as a function of age, sex, body condition, etc., and these changes may influence partitioning.

Mechanism of Action of Inhaled Anesthetics The specific mechanism of action of most anesthetics remains unknown. Volatile anesthetics appear to share some common cellular actions with other sedative, hypnotic, or analgesic drugs. A sound theory of anesthetic action should provide an explanation for the observed correlation of potency with the oil/gas partition coefficient, the observation that a large number of diverse chemical structures can cause anesthesia, and explain why the agents produce side effects. Experimental work has implicated a protein "target" on a diverse population of ionophores that is required for anesthetic action (Franks and Lieb, 2004). The alteration in ionophore conductance may be related to direct binding of the anesthetic at a 2-amino-acid sequence within the trans-membrane spanning domains.

The protein receptor hypothesis postulates that protein receptors in the CNS are responsible for the mechanism of action of inhaled anesthetics. This theory is supported by the steep dose-response curve for inhaled anesthetics. However, it remains unclear if inhaled agents disrupt ion flow through membrane channels by an indirect action on the lipid membrane, via a second messenger, or direct and specific binding to channel proteins. Another theory describes the activation of gamma-aminobutyric acid (GABA) receptors by the inhalation anesthetics. Volatile agents may activate or facilitate GABA channels, resulting in hyperpolarized

Table 1.2. Selected partition coefficients of commonly used anesthetic agents.

Anesthetic	Blood:Gas Partition Coefficient	Brain:Blood Partition Coefficient
Nitrous oxide	0.47	1.1
Desflurane	0.42	1.3
Enflurane	1.4	1.4
Sevoflurane	0.69	1.7
Methoxyflurane	12.0	2.0
Isoflurane	2.6	2.7
Halothane	2.9	2.9

Adapted from: Steffey EP. Inhalation anesthetics. In: Thurmon JT, Tranquilli WJ, Benson GJ, eds. *Lumb and Jones' Veterinary Anesthesia*, 3rd ed. Baltimore: Williams & Wilkins, 1996.

cell membranes. In addition, they may inhibit certain calcium channels, preventing the release of neurotransmitters and inhibit glutamate channels.

Evidence for the protein receptor theory includes the observation made by Franks and Lieb that a broad range of inhalant anesthetics inhibited the water-soluble enzyme firefly luciferase (Franks and Lieb, 1984). This enzyme hydrolyzes luciferin to create light and is often a model for anesthetic action because the rank orders of potency of the anesthetics in animals parallels that of luciferase inhibition. Franks and Lieb studied the enzyme in a lipid-free environment, with only the enzyme present, and observed the enzyme could be completely inhibited. This suggests the site of action is within the protein structure and is not strictly dependent on lipid. Franks and Lieb also noted that some anesthetics exist as stereoisomers and that the effects of these isomers can differ. However, when the stereoisomers are introduced into a lipid substrate the physical effects on the lipid are identical. This is further evidence that the anesthetic is acting at a stereoselective "receptor" and implicates a protein as the site of action.

Following up on the work by Franks and Lieb, Mihic and colleagues attempted to reconcile the apparent problem of the non-specific action of anesthetics on a wide range of protein channels, including glycine, glutamate, GABA, and other neurotransmitter activated channels (Mihic et al., 1997). For the anesthetic to act on all of these channels, one would expect that a target amino acid sequence would be conserved among all channels or the anesthetic would be altering receptor function by distorting the surrounding environment. In their experiments, this group began making chimeric DNA encoding the c-terminal human GABA rho receptor subunit, which is an anesthetic insensitive receptor, and the N-terminal glycine-binding part of the human glycine α -receptor subunit that is situated in the transmembrane spanning domain. They expressed the cDNA in Xenopus oocytes and measured resulting chloride conductance. They determined the site of anesthetic action was within the N-terminal sequence of the third transmembrane spanning domain. The researchers then began to construct cDNA containing point mutations within this region and created receptors that were insensitive to enflurane. They ultimately found two amino acids in the glycine receptor that abolished enflurane sensitivity when mutated. Changing the corresponding amino acids on the GABA receptor also abolished enflurane sensitivity. However, these mutations did not reduce the receptor's sensitivity to the injectable anesthetic propofol.

Inhalant Anesthetic Pharmacokinetics

Anesthetic Uptake and Distribution A series of partial pressure gradients, beginning at the vaporizer; continuing in the anesthetic breathing circuit, the airways, alveoli, blood; and ending in the tissues drives the

movement of an anesthetic gas. The movement of that gas continues until equal partial pressures are present throughout the system. Because the lung is the point of entry and exit to the body, the alveolar partial pressure governs the partial pressure of the anesthetic in all body tissues. Therefore, it is most important to understand how to influence the alveolar partial pressure. Increasing alveolar minute ventilation, flow rates at the level of the vaporizer, and inspired anesthetic concentration, can speed the delivery of anesthetic and increase the rate of rise of alveolar anesthetic partial pressure. Solubility, cardiac output, and the alveolarvenous anesthetic gradient are factors that determine the uptake of the anesthetic from the alveoli into the blood. Solubility describes the affinity of the gas for a medium such as blood or adipose tissue and is reported as a partition coefficient. The blood-gas partition coefficient describes how the gas partitions itself between the two phases (blood and alveolar gas) after equilibrium has been reached. Isoflurane, for example, has a bloodgas partition coefficient of approximately 1.4 (Steffey, 1996). This means that if the gas partial pressures are in equilibrium, the concentration in blood will be 1.4 times greater than the concentration in the alveoli. A higher blood-gas partition coefficient means a greater uptake of the gas into the blood; therefore, a slower rate of rise of alveolar and blood partial pressure. Because the blood partial pressure rise is slower, it takes longer for the brain partial pressure of the gas to increase, resulting in a longer induction time.

Increased cardiac output exposes the alveoli to more blood per unit time. The greater volume of blood removes more inhalant anesthetic from the alveoli, therefore lowering the alveolar partial pressure. The agent might be distributed faster within the body, but the partial pressure in the arterial blood is lower. It takes longer for the gas to reach equilibrium between the alveoli and the brain; therefore, a high cardiac output usually prolongs induction time. The alveolar-venous partial pressure difference reflects tissue uptake of the inhaled anesthetic. A large difference is caused by increased uptake of the gas by the tissues during the induction phase.

Transfer of the gas from the arterial blood into tissues such as the brain depends on perfusion and the relative solubility of the gas in the different tissues. The brain-blood coefficient describes how the gas partitions itself between the two phases after equilibrium has been reached. Isoflurane has a brain-blood coefficient of 2.7; therefore, when the system is at equilibrium the concentration in the brain is 2.7 times greater than the concentration in the blood (Steffey, 1996). All contemporary inhalation anesthetics have high adipose-blood partition coefficients. This means that most of the gas accumulates in adipose tissue as times goes by. The partial pressure of the gas in adipose tissue rises very slowly because this tissue has a high capacity (as indicated by

the high adipose-blood partition coefficient). Inhalation anesthetics stored in obese patients may delay awakening at the end of long periods of anesthesia. Fortunately, adipose tissue has a relatively low blood flow and does not accumulate significant amounts of anesthetic during the short periods of anesthesia commonly encountered in veterinary medicine.

Elimination of Inhaled Anesthetics The rate of induction and recovery from anesthesia with inhalant anesthetics differs between agents because of differences in tissue solubility; however, general statements can be made. During induction all tissue partial pressures are zero. During recovery, different tissues in the body have different partial pressures of anesthetic that are governed by the tissue anesthetic content and not the alveolar partial pressure. Recovery is not as controllable as induction of anesthesia. During recovery from anesthesia, elimination occurs through exhalation and biotransformation.

Enzymes responsible for inhalant anesthetic metabolism are mainly located in liver and kidneys. Anesthetic elimination via metabolism is approximately 50% for methoxyflurane, 10% to 20% for halothane, 5% to 8% for sevoflurane, 2.5% for enflurane, about 0.2% for isoflurane, 0.001% for desflurane, and nearly 0% for nitrous oxide (Steffey, 1996). The amount of anesthetic eliminated from the body during anesthesia because of metabolism is small compared with the amount exhaled. However, anesthetic metabolism accounts for a larger proportion of the anesthetic clearance after anesthetic delivery ceases. The low, but prolonged, blood partial pressure of the anesthetic found after terminating delivery is no longer overwhelming the enzyme systems (enzymes become saturated above approximately 1 MAC) so metabolism accounts for a larger proportion of clearance than it did during exposure to high partial pressures.

Elimination of the anesthetic via the lungs can be complex. The first point to consider is what effect an increase in alveolar minute ventilation will have on recovery. During recovery, increasing minute ventilation will decrease alveolar anesthetic partial pressure and increase the gradient for diffusion from the blood to the alveoli. This increases elimination, especially for most anesthetic agents with high blood-gas partition coefficients.

Another situation to consider is what effect a change in cardiac output will have on the rate of decrease of partial pressure of the inhalant anesthetic. During induction, high cardiac output increases the rate at which anesthetic is removed from the lung, slowing the rate of rise of anesthetic partial pressure, slowing induction. When cardiac output is reduced (e.g., cardiogenic shock) there is a slower removal of anesthetic and subsequently a faster rate of rise of alveolar partial pressure and induction occurs. During recovery a high cardiac

output will increase the rate at which anesthetic is returned to the lung for excretion. Because the partial pressure of anesthetic in the blood is determined by the tissues, the higher blood flow shortens recovery. During low cardiac output situations there is a slower recovery because of the decreased rate at which tissue anesthetic partial pressure decreases.

The last major influence on the rate of induction and recovery is the solubility of the anesthetic agent. Agents with high blood-gas solubility are partitioned into the blood to a greater extent than agents with low blood-gas solubility. The blood acts as a depot for agents maintaining anesthetic partial pressure. Agents with low blood-gas solubility do not partition into the blood to the extent of highly soluble agents; thus, the decrease in partial pressure is faster and recovery time is reduced. Highly soluble agents have high blood concentrations and it takes longer for the partial pressure to decrease if all other factors are equal. In summary, elimination of a volatile anesthetic depends on ventilation, cardiac output, and solubility of the gas in blood and tissue.

Control of the Partial Pressure of Delivered Anesthetic

Inhalant anesthetics can be classified as either gaseous (nitrous oxide, xenon) or volatile (isoflurane, sevoflurane, halothane, methoxyflurane, and desflurane). Gaseous anesthetics are usually delivered to the anesthesia machine under pressure and their rate of delivery to the breathing circuit is controlled by a flow meter. Volatile anesthetics are liquids at room temperature and pressure, and usually are delivered by a specialized apparatus that controls the volatilization of the liquid, and proportioning of the vapor in the fresh gas delivered to the patient. A vaporizer can be as simple as a piece of cotton soaked with agent held near the nose (not recommended) or can be as complex as the Tec 6 vaporizer for desflurane.

The Breathing System With most modern anesthetic machines, the outflow gas from the vaporizer is delivered to the patient through a set of tubes and machinery collectively called a breathing system. There are many styles of breathing systems, each with a multitude of uses. It is important that the anesthetist understands how the type of breathing circuit used will impact the rate at which the anesthetic concentration can be changed and the relationship between the vaporizer setting and inspired concentration.

Waste Anesthetic Gases The health effects of chronic exposure to waste anesthetic gases are not completely known. The frequency of inhalant anesthetic use and the lack of significant associations between exposure and most types of chronic toxicities (e.g., cancer, infertility, birth defects, etc.) suggest there is only a very low risk (if any) associated with chronic exposure. However,

certain individuals are highly susceptible to potentially life-threatening reactions, even with trace level exposure (e.g., malignant hyperthermia). In light of this, and with the admission that we do not completely understand all the risks associated with chronic exposure, it is generally agreed that the exposure of personnel be kept as low as reasonably acceptable (ALARA). In the United States, the Occupational Safety and Health Administration (OSHA) requires veterinary hospitals to maintain a system to prevent waste gases from building up in the area of use and can enforce exposure limits that are consistent with recommendations offered by the National Institute of Occupational Safety and Health (NIOSH). The NIOSH recommends that the maximum time-weighted average concentration of volatile halogenated anesthetics should not exceed 2 ppm when used alone or 0.5 ppm when used with nitrous oxide and that nitrous oxide concentration should not exceed 25 ppm (American College of Veterinary Anesthesiologists, 1996).

Minimum Alveolar Concentration

The measurement of the dose of an inhalant anesthetic is the minimum alveolar concentration (MAC) multiple. It is defined as the minimum alveolar concentration at 1 atmosphere, required to prevent gross purposeful movement in 50% of the subjects tested, following a 60-second application of a supramaximal stimulus (Steffey, 1996). One MAC is by definition the EC_{50} (i.e., effective concentration in 50% of patients) for that agent. Animals awaken from anesthesia at approximately 0.5 MAC, surgical anesthesia occurs at approximately 1.3 MAC, and severe autonomic nervous system depression occurs around 2 MAC. Birds and many reptiles do not have true alveoli so the concept of MAC has been modified or redefined to be the minimum anesthetic concentration. It is not identical to MAC from other species, but closely approximates it in many ways.

Physiological and Pharmacological Factors that Alter MAC Minimum alveolar concentration is age dependent, being lowest in newborns, reaching a peak in infants, and then decreasing progressively with increasing age (Lerman, 1983, 1994; Taylor and Lerman, 1991). Increases in MAC can also occur from hyperthermia and hypernatremia and decreases in MAC can result from hypothermia, hyponatremia, pregnancy, hypotension, and drugs such as lithium, lidocaine, opioids, and α -2 adrenergic agonists.

General Pharmacological Actions of Inhalant Anesthetics

Inhalant anesthetic agents have more similarities than differences with respect to their effects on vital organ systems. The differences are primarily related to the speed and magnitude with which the changes occur. There are a few classic differences that have been included in the following synopsis.

Central Nervous System All inhalant general anesthetics alter consciousness, memory, and pain perception by acting on the CNS. Most inhalant anesthetics cause a mild to moderate decrease in the cerebral metabolic requirement for oxygen (CMRO₂) and they usually have minimal effects on cerebral blood flow autoregulation at low MAC multiples (Mielck et al., 1998, 1999). Patients with intracranial hypertension should not be anesthetized with nitrous oxide because it may cause an increase in CMRO₂ (Roald et al., 1991; Algotsson et al., 1992; Hoffman et al., 1995). Halothane is also a poor choice because of its significant effects on cerebral blood flow autoregulation (Steffey, 1996). Isoflurane, sevoflurane, and desflurane are the inhalants of choice at this time.

Cardiovascular System Most inhalant anesthetic agents cause direct myocardial depression. Halothane is the most effective depressant on contractility; however, it generally has the fewest effects on vascular resistance (Steffey, 1996). Isoflurane, enflurane, sevoflurane, and desflurane cause some degree of vasodilatation, which tends to improve forward blood flow and maintain tissue perfusion. The reduction in afterload also tends to offset some of the direct myocardial depressant effects and may result in a net improvement in cardiac output. Nitrous oxide is a sympathomimetic and can improve contractility, blood pressure, and heart rate at light levels of anesthesia. Rapid changes in anesthetic concentration (especially with desflurane) may result in a sympathetic response and temporarily increase cardiac work.

Respiratory System All anesthetics tend to depress the chemoreceptor response to carbon dioxide, leading to an accumulation of carbon dioxide and a respiratory acidosis unless ventilation is assisted or controlled. The ether derivatives tend to be the most depressant; however, all agents may cause significant depression. Most inhalant agents may interfere with hypoxic pulmonary vasoconstriction and may worsen ventilation-perfusion matching in the lung. This is most dramatic in larger animals, in which significant pulmonary shunting is often observed.

Genital-Renal Systems Most anesthetics cause a decrease in renal perfusion and an increase in the anti-diuretic hormone (ADH) secretion. Inhalant anesthetics may be the safest anesthetic techniques in anuric renal failure since pulmonary excretion is not dependent upon renal function.

Inhalant anesthetics may cause an increase in postpartum uterine bleeding. This is a bigger consideration in primate anesthesia because of placentation characteristics. Isoflurane, sevoflurane, desflurane, and nitrous oxide have been advocated for use during Caesarian section because of the rapid onset and termination of effect, and the transient effects on the delivered fetuses. Methoxyflurane and halothane are less desirable because of their greater solubility and slower elimination.

Clinically Useful Inhalant Anesthetics

Nitrous Oxide Nitrous oxide is commonly used in combination with a primary inhalant or injectable anesthetic drug. The reason it is not useful in veterinary anesthesia as a solo anesthetic is because of its low potency. Nitrous oxide's MAC value has been estimated to be near 100% for humans and closer to 200% for veterinary patients. It is obvious that 200% nitrous oxide cannot be delivered; in fact, no more than 79% nitrous oxide can be safely delivered without creating a hypoxic gas mixture. In practice it is common to use a 50% nitrous oxide mixture with the balance of the mix being oxygen. If 50% nitrous oxide is delivered to an animal it is only providing approximately 0.25 MAC of anesthesia. A potent volatile anesthetic, injectable agent or other sedative/analgesic drug must supply the remaining 0.75 MAC. Because of this limited anesthetic effect, nitrous oxide use for anesthetic maintenance is not widespread in veterinary medicine. Nitrous oxide is used by some anesthetists during induction of anesthesia for the second gas effect. Because nitrous oxide is present in the inspired gas mixture in a relatively high concentration and it rapidly diffuses into the body from the alveoli, the rate of rise of partial pressure of a second co-administered inhalant anesthetic is increased and induction time can be shortened.

Nitrous oxide has a low blood-gas partition coefficient and has a rapid onset and recovery. The gas can diffuse out of the blood so rapidly that if nitrous oxide delivery is suddenly halted and supplemental oxygen is not administered, a situation known as diffusion hypoxia may result. Diffusion hypoxia happens when the mass movement of nitrous oxide down its partial pressure gradient results in high alveolar nitrous oxide partial pressure at the expense of oxygen and nitrogen partial pressures. Because breathing room air results in an alveolar oxygen partial pressure of approximately 100 mmHg under ideal circumstances, any displacement of oxygen by nitrous oxide results in alveolar hypoxia. Diffusion hypoxia can be minimized or prevented by continuing the administration of oxygen enriched gas for 5 to 10 minutes following the discontinuation of nitrous oxide. This helps because during normal breathing, 100% oxygen should result in an alveolar oxygen partial pressure close to 500 mmHg. The partial pressure of oxygen can drop a lot further before hypoxia

Nitrous oxide is contraindicated in animals with pneumothorax, gastric dilatation, gas embolism, and other conditions that are exacerbated by accumulation of gas inside a closed space. This effect is caused by diffusion of nitrous oxide out of the blood into the preexisting

gas space in an attempt to establish equilibrium. Nitrous oxide is also contraindicated in animals with gas diffusion impairment such as interstitial pneumonia. These animals typically have low arterial oxygen partial pressure when breathing oxygen rich mixtures. The dilution of oxygen by nitrous oxide will lower the inspired oxygen partial pressure and may worsen hypoxemia.

Halothane Halothane was a major advancement in inhalant anesthesia in its day. It was introduced in the late 1950s and was potent, non-irritating, and nonflammable. Chemically it is classified as a halogenated hydrocarbon and it is not chemically related to the ethers. Halothane was used widely in human anesthesia until it became apparent there were potentially fatal adverse effects associated with its use. Human patients developed a syndrome known as halothane hepatitis (Neuberger, 1998; Daghfous et al., 2003). This rare, but life-threatening complication is still something of a mystery, although an immunological etiology is implicated. The disease appears as a fulminant hepatitis, similar to that seen with viral hepatitis, which develops after a short period of apparent recovery. A second more common form of hepatitis is less severe and is characterized by a reversible elevation in liver enzymes. The etiology of this second form is thought to be anesthetic-related hepatic hypoxia and does not appear to be immune related. Diagnosis of the correct form is important because a repeated exposure to halothane, or any of the volatile agents producing trifluoroacetic acid, is more likely to trigger the immunologically mediated form and result in high morbidity and mortality. Both forms are not commonly documented in veterinary patients; however, transient elevation of liver enzymes may occur postoperatively in some patients. A thorough diagnostic workup is required because of the non-specific and multifactorial etiology of elevated liver enzymes.

A second complication associated with halothane anesthesia is the development of arrhythmias. Halogenated hydrocarbon anesthetics, especially halothane, can sensitize the myocardium to the arrhythmogenic effects of epinephrine. Halothane is generally contraindicated in patients who are predisposed to ventricular arrhythmias (e.g., hypoxia, trauma, or myocardial disease) (Steffey, 1996). Arrhythmias that develop during halothane anesthesia may resolve when the anesthetic agent is switched to isoflurane or sevoflurane. Other causes of perianesthetic arrhythmias also should be ruled out.

Halothane undergoes extensive hepatic metabolism (approximately 20%) and is not chemically stable (Steffey, 1996). Commercially available halothane contains thymol, a preservative, which does not volatilize to the same degree as halothane. This results in a sticky residue inside the vaporizer that should be cleaned out during periodic maintenance. Veterinary use of

halothane is declining as a result of the increasing popularity of isoflurane and sevoflurane and its limited availability worldwide.

Isoflurane Isoflurane is arguably the most widely used veterinary inhalant anesthetic in the world today. Isoflurane is stable and potent, and undergoes little metabolism. Isoflurane can be irritating to airway tissues at high-inspired concentrations and its use for induction in people has been limited because of patient complaints and complications. However, in veterinary medicine isoflurane mask induction is still common. Isoflurane is a potent agent (MAC approximately 1.3% in dogs) and has a high saturated vapor pressure (approximately 240 mmHg at room temperature) (Steffey, 1996). These characteristics coupled with the fact that it is possible to cause rapid partial pressure changes in the brain suggest that only precision vaporizers located outside the circuit (VOC) should be used to deliver the agent. However, several reports of the use of modified vaporizers located inside the circuit (VIC) suggest that this type of anesthetic system can be used to safely administer the agent (Bednarski, Gaynor, and Muir, 1993; Laredo et al., 1998).

Isoflurane metabolism is minimal (less than 1%) and fluoride induced nephrotoxicity is uncommon. Isoflurane (and many of the ether-derivative volatile agents) are excellent vasodilators and can cause or worsen hypotension. Administration of fluids and/or sympathomimetic agents can usually counteract the observed hypotension. Likewise, administering preanesthetic drugs (e.g., opioids), which reduce the amount of inhalant required, also reduce the degree of vasodilation.

Desflurane Desflurane use in veterinary medicine is limited to academic institutions and a very limited number of private practices. The main disadvantage to desflurane use is cost associated with the agent and the cost associated with a specialized vaporizer that is required to deliver the drug. Desflurane is extremely insoluble and is capable of producing extremely rapid inductions and recoveries (Clarke, 1999; Barter et al., 2004). Its main market is for human outpatient anesthesia, in which rapid recovery is a large cost savings. It is highly fluorinated, has a very low potency (MAC approximately 9%), and has a high saturated vapor pressure (approximately 670 mmHg at room temperature) (Steffey, 1996). Desflurane boils at 23°C and must be handled using a specialized apparatus for vaporizer filling. The vaporizer is specific for desflurane and is electrically heated to boil the desflurane so that a reliable vapor pressure will be produced. Then sophisticated differential pressure transducers and electronic circuits calculate an injection ratio for delivery of the desired anesthetic concentration. Desflurane is very stable and undergoes almost no metabolism.

Sevoflurane Sevoflurane is the newest volatile inhalant anesthetic approved for veterinary use. Sevoflurane has a low blood-gas partition coefficient (approximately 0.7), which is greater than desflurane and nitrous oxide, but about half that of isoflurane. Extensive pulmonary elimination of sevoflurane minimizes the amount available for metabolism. Up to 3 to 8% of the sevoflurane dose is metabolized and appears in the urine as inorganic fluoride (Steffey, 1996). This fluoride exposure does not appear to be clinically significant, although serum levels of fluoride can approach those previously reported to be nephrotoxic for methoxyflurane. Factors other than peak serum fluoride concentrations appear important for predicting the incidence of nephrotoxicity (Driessen et al., 2002).

Sevoflurane represents a deviation from the methyl ethyl ether structural theme present in other contemporary volatile anesthetics. Sevoflurane is chemically related to methyl-isopropyl ethers. The structure is significant because an important metabolite of most methyl-ethyl ether volatile anesthetic agents (trifluoroacetic acid) is a suspected trigger of halothane hepatitis. Sevoflurane cannot be metabolized to form this compound. This is not a major consideration in veterinary medicine, but is important in human anesthesia. Sevoflurane is also pleasant and non-irritating when used for mask induction and many pediatric anesthesiologists suggest this agent is the drug of choice for pediatric induction via mask. Sevoflurane is less potent than isoflurane (MAC approximately 2.3% for dogs and horses). When used for induction of anesthesia it is common to use 7% to 9% sevoflurane.

An early subject of controversy surrounding sevoflurane anesthesia was the production of compound A. Compound A is a degradation product produced when sevoflurane reacts with the carbon dioxide absorbent. Early toxicology studies performed in rats suggested that proximal tubular renal damage could result from clinically relevant exposure to compound A. This led to the suggestion that sevoflurane should not be used in closed circuit anesthesia or with fresh gas flow rates lower than 2 L/min. However, since that time little clinical evidence of renal damage in humans and dogs has emerged, even with very low fresh gas flows. Some have suggested that rats have a 10 to 100 times higher level of an enzyme β -lyase that is believed to convert the intermediate compounds of Compound A metabolism to a nephrotoxic molecule (Sheffels et al., 2004; Kharasch et al., 2005). Humans and dogs do not appear

to have the same level of enzyme conversion and are therefore less susceptible to Compound A toxicity. Safety studies in most other rodents and exotic animals are not published and caution should be used when administering sevoflurane via a circuit breathing system until further safety data are available (Table 1.3).

INJECTABLE ANESTHETICS

Injectable anesthetics are an important family of compounds used for immobilization and anesthesia of wildlife. The dissociative anesthetics in particular are commonly combined with other adjunctive drugs such as α_2 -adrenergic agonists and opioids to improve reliability and speed of onset of action.

Barbiturates

Barbiturates can be classified in several ways. One is by chemical structure. Oxybarbiturates are historically important, but not commonly used today because of their slower onset of action, long recovery characteristics, and relatively small margin of safety. Pentobarbital is the protypical oxybarbiturate. It has been combined with several adjunctive drugs for anesthesia. The thio (i.e., sulfur substituted) analog of pentobarbital, thiopental, is still used by intravenous (IV) administration for induction of anesthesia in domestic animals. However, perivascular injection can result in tissue necrosis and its use in non-domestic species is limited because of the inability to obtain reliable IV access prior to anesthetic induction.

Barbiturates cause anesthesia through global depression of CNS activity. This is accomplished through interference with nervous system impulse conduction. Like many other anesthetics, other excitable tissues can be affected resulting in commonly encountered side effects, including depression of cardiorespiratory function. Barbiturates decrease cerebral blood flow (CBF) and CMRO₂. Cerebral metabolic requirement for oxygen decreases progressively until electroencephalographic activity becomes isoelectric (Branson, in press).

Propofol

Propofol (2,6-diisopropylphenol) is commonly used for sedation, induction, and maintenance of anesthesia in humans and domestic species. Propofol is supplied as a milky white liquid for IV injection. It is insoluble in aqueous solution; therefore, it is usually formulated as an emulsion of 10% soybean oil, 2.25% glycerol, and

Table 1.3. Structure and characteristics of inhalation anesthetics.

Agent	Year Introduced	Structure	Agent Type
Halothane	1956	CF ₃ -CHClBr	Alkane
Isoflurane	1981	CF ₃ CHCl-O-CHF ₂	Ether
Enflurane	1972	CHClF-CF ₂ -O-CHF ₂	Ether
Methoxyflurane	1960	CHCl ₂ -CF ₂ -O-CH ₃	Ether
Desflurane	1992	CF ₃ CHF-O-CHF ₂	Ether

1.2% egg phosphatide. Some formulations of propofol (e.g., Diprivan, Propoflo, and Rapinovet) do not contain preservatives, and support bacterial and fungal growth if the drug becomes contaminated. This has led to the label recommendation of discarding unused drug at the end of the procedure or within 6 hours of opening a vial. Some formulations have additives such as sulfites or benzyl alcohol to improve stability or reduce the potential of accidental contamination. Species sensitivities to these additives should be investigated before their use (Davidson, 2001).

Propofol is classified as an ultrashort-acting injectable anesthetic agent. Duration of effect is typically 5 to 10 minutes in dogs and 5 to 20 minutes in cats. Its rapid recovery characteristics are maintained in most species following prolonged infusions. Recovery times may be prolonged in the cat (and other species that have reduced capacity for glucuronidation of drugs) following repeated doses or continuous rate infusions.

Propofol has been used in dogs, cats, horses, pigs, goats, sheep, and even birds. Wild turkeys, mallard ducks, pigeons, and chickens have been anesthetized with propofol, but there is significant cardiorespiratory depression in ducks and chickens indicating birds may need ventilatory support during anesthesia (Machin and Caulkett, 1998). Apnea and respiratory depression are the best known side effects of propofol administration. The incidence of apnea may be reduced by administering the drug over 60 to 90 seconds (Muir and Gadawski, 1998). It is prudent to be prepared to intubate and support ventilation if apnea occurs. Pain is reported on propofol injection by some people. Muscle fasciculations and spontaneous twitching can occur in some animals.

Dissociative Anesthetics

Ketamine Veterinary formulations of ketamine are a racemic mixture consisting of two optical enantiomers. The *S* enantiomer is less cardiodepressant and has a fourfold greater affinity for the phencyclidine site in the *N*-methyl-D-aspartate (NMDA) receptor. Serotonin transport is inhibited twofold by the *R* form. Some of ketamine's effects are not stereoselective. Norepinephrine release is equivalent from the *S* and *R* forms (Kohrs and Durieux, 1998).

Ketamine can be administered intramuscularly to anesthetize animals that are not easily given drugs intravenously. Intramuscular (IM) administration produces a longer duration of anesthesia than IV administration, but the recovery is usually longer and can be accompanied by more dysphoria. Recovery from ketamine appears to be caused by redistribution and metabolism similar to the thiobarbiturates. Hepatic biotransformation to norketamine (metabolite I) and dehydronorketamine (metabolite II) is the major route of metabolism in most species studied. It was thought ketamine was excreted unchanged in the urine of cats; however, this originated from one paper published in 1978 by Gaskell et al. and since that time it has been shown by

Waterman that biotransformation is an important route of elimination in domestic cats (Waterman, 1983). Norketamine is about one-third to one-fifth as potent as the parent compound but may contribute to the prolonged analgesic effects of ketamine (Kohrs and Durieux, 1998).

Ketamine produces a form of anesthesia that is different from other hypnotic drugs. In general terms, ketamine induces anesthesia and amnesia by functional disruption (dissociation) of the CNS through marked CNS stimulation, resulting in catalepsy, immobility, amnesia, and marked analgesia. Electroencephalographic analysis indicates that depression of the thalamoneocortical system occurs in conjunction with activation of the limbic system. Awakening from ketamine anesthesia in people is frequently characterized by disagreeable dreams and hallucinations. Sometimes these unpleasant occurrences may recur days or weeks later. Almost half of adults over the age 30 exhibit delirium or excitement or experience visual disturbances. The occurrence of adverse psychological experiences is much lower in children. The incidence of adverse psychological experiences in animals is unknown; however, a significant number of animals transiently vocalize and have motor disturbances during recovery.

Ketamine's neuropharmacology is complex. The compound interacts with NMDA and non-NMDA glutamate receptors, nicotinic, muscarinic cholinergic, monoaminergic, and opioid receptors. In addition there are interactions with voltage-dependent ion channels such as Na⁺ and L-type Ca²⁺ channels. It is believed that the NMDA receptor antagonism accounts for most of the analgesic, amnestic, psychomimetic, and neuroprotective effects of the compound, but the exact mechanism of its anesthetic action is not known. NMDA receptor activation is believed to play a role in the "memory" of the CNS, which is involved in the windup, hyperalgesia, and allodynia seen in certain pain syndromes (Kohrs and Durieux, 1998).

Ketamine can increase the CMRO₂ because of increased metabolic activity associated with increased activity in certain areas of the brain. Intracranial pressure (ICP) also increases, possibly because of two mechanisms: (1) Ketamine can increase mean arterial blood pressure, so CBF can increase and ICP passively increase in patients with altered autoregulation; and (2) ketamine can depress respiration increasing PaCO₂. The brain responds to elevations in PaCO₂ by increasing CBF, which increases ICP. Ventilation may reduce the increase in CBF. Current clinical dogma dictates avoiding ketamine in patients with suspected head trauma.

Ketamine causes a characteristic breathing pattern termed *apneustic breathing*, characterized by prolonged inspiratory duration and relatively short expiratory time. When ketamine is administered by itself, it typically causes minimal respiratory depression that is short lived. Hypoxic and hypercapnic respiratory regulation appears to remain intact. However, ketamine is seldom

given alone. It is often combined with benzodiazepines, acepromazine, opioids, or α_2 -adrenergic agonists. The combined effect of these drugs is usually decreased minute ventilation, increased PaCO₂, and mild respiratory acidosis.

When given to animals with functioning sympathetic nervous systems, ketamine generally increases heart rate and arterial blood pressure. Cardiac output usually stays the same or slightly increases. Ketamine is seldom given alone to healthy animals. The use of adjunctive drugs such as benzodiazepines, acepromazine, or α_2 -adrenergic agonists tends to blunt the sympathomimetic effect of ketamine and tends to decrease cardiac function and decrease arterial blood pressure.

Telazol Telazol is a non-narcotic, non-barbiturate, injectable anesthetic agent. Chemically, Telazol is a combination of equal parts by weight of tiletamine hydrochloride (2-[ethylamino]-2-[2-thienyl]-cyclohexanone hydrochloride), an arylaminocycloalkanone dissociative anesthetic, and zolazepam hydrochloride (4-[o-fluorophenyl]-6,8-dihydro-1,3,8-trimethylpyazolo[3,4-e][1,4]diazepin-7[1H]-1-hydrochloride), a benzodiazepine having minor tranquilizing properties. The product is supplied sterile in vials, each containing a total of 500 mg of active drug as free base equivalents and 288.5 mg mannitol. The addition of 5 ml diluent produces a solution containing the equivalent of 50 mg tiletamine base, 50 mg zolazepam base, and 57.7 mg/ml mannitol. The resulting solution has a pH of 2 to 3.5.

Telazol's duration of effect is dependent upon route of administration and amount of drug given. When used intravenously it lasts approximately 15 to 20 minutes. When given intramuscularly it may last 30 to 45 minutes. It is commonly used in place of ketamine and its duration is typically longer.

Tiletamine induces dissociative anesthesia similar to ketamine. It has the potential to cause seizure activity; however, when combined with zolazepam the incidence of seizures is greatly reduced. Its effects on CBF and ICP are similar to those of ketamine. Nephrotoxicity in New Zealand white rabbits has been reported following Telazol administration (Doerning et al., 1992). Anecdotally, tigers do not appear to recover well after Telazol; therefore, its use is generally contraindicated. Telazol can be combined with other drugs to improve its analgesic and recovery characteristics.

Miscellaneous Anesthetics

Etomidate Etomidate has been used extensively as a hypnotic agent for the induction of anesthesia in humans, but less commonly in other species. Etomidate is a rapidly acting, ultrashort-acting imidazole derivative. The duration of effect following IV bolus administration is typically 5 to 10 minutes. Etomidate causes dose-dependent CNS depression leading to sedation, hypnosis, and finally an isoelectric electroencephalogram.

Etomidate, in contrast to almost all other induction agents, does not seem to cause significant depression of cardiac contractility and has minimal effects on heart rate, cardiac output, and arterial blood pressure. Elimination of etomidate occurs by ester-hydrolysis in plasma and in the liver at approximately equal rates. Metabolism of etomidate in the liver is a capacitylimited Michaelis-Menten process. Hepatic hydrolysis results in the corresponding inactive carboxylic acid. Etomidate temporarily reduces steroidogenesis (Boidin, 1985; Moon, 1997). Steroid synthesis usually increases with the stress of anesthesia, so the net effect may be little or no change (Dodam et al., 1990). It is not a clinical contraindication except for animals with hypoadrenocorticism (Addison's disease). IV administration of etomidate may induce excitement, myoclonus, pain on injection, vomiting, and apnea during induction of anesthesia. Some animals may have purposeless myoclonic muscle movements during recovery from anesthesia. The frequency and severity of the side effects can be attenuated or eliminated by the administration adjunctive drugs such as diazepam, acepromazine, or opioids prior to etomidate administration. A constant rate infusion of etomidate may result in hemolysis (Moon, 1994; Van de Wiele et al., 1995). This is thought to result from the propylene glycol carrier (Doenicke et al., 1997).

Alphaxalone/Alphadolone

Saffan Alphaxalone is a steroid anesthetic with a relatively wide margin of safety, little cardiovascular or respiratory depression, and minimal induction and recovery excitement. Alphaxalone is poorly soluble in water, so to improve solubility it is formulated with another steroid, alphadolone acetate, which also has anesthetic activity. The addition of alphadolone increases the water solubility of alphaxalone threefold. One commercially available formulation, Saffan, is a mixture of alphadolone, alphaxalone, and Cremophor EL. The Cremophor is a non-ionic surfactant that makes the aqueous solution possible; however, Cremophor can cause histamine release and severe cardiovascular adverse events in some species (e.g., domestic dog). The main route of elimination is by biotransformation in the liver and secretion in the bile.

Alfaxan CD Alphaxalone is available in Australia as a novel formulation that uses cyclodextrin as a solvent rather than Cremophor EL. The resulting compound lacks the histamine-releasing properties of Saffan, yet retains the safety and efficacy of alphaxalone.

OPIOIDS

All drugs classified as opioids are chemically related to a group of compounds that have been purified from the juice of a particular species of poppy, *Papaverum*

somniferum. The unrefined extract from the poppy is called opium and contains approximately 20 naturally occurring pharmacologically active compounds, including morphine and codeine. In addition, numerous semisynthetic and synthetic analogs of these natural compounds have been developed for clinical use. The word *opioid* is typically used to encompass all chemical derivatives of the compounds purified from opium and is the term used to describe this class of analgesics throughout this section.

The opioids are a versatile group of drugs with extensive applications related to the management of pain in companion animal veterinary medicine. In the past, their use in wild and exotic species has been largely limited to the ultra-potent agents used in remote capture techniques. However, with the rapid evolution of zoo animal medicine and surgery, the opioids are being used increasingly as analgesics for the management of surgical pain in a wide variety of species. Although there are few pharmacokinetic or pharmacodynamic studies involving opioids in wild and exotic animals, a general discussion of opioid pharmacology is relevant and may facilitate extrapolation from companion animal species.

Opioid Receptors

It is well known that exogenously administered opioids such as morphine or heroin exert their effects by interacting with specific opioid receptors and mimicking naturally occurring molecules known as endogenous opioid peptides. Based on work carried out over the past 20 years, it is now accepted that there are three welldefined types of opioid receptors, most commonly known by their Greek letter designations as μ (mu), δ (delta), and κ (kappa) (Harrison, Kastin, and Zadina, 1998; Kieffer, 1999; Inturrisi, 2002; Janecka, Fichna, and Janecki, 2004). This classic system of nomenclature has been under reconsideration for a number of years. During this time several alternative naming systems have been proposed leading to considerable confusion. In addition, a fourth type of opioid receptor, the nociception receptor (also known as the orphanin FQ receptor) has been characterized recently (Moran, Abdulla, and Smith, 2000; Smith and Moran, 2001). According to the most recent recommendations of the International Union of Pharmacology subcommittee on nomenclature, variations based on the Greek letters remain acceptable. Thus, mu, μ, or MOP (for mu opioid peptide); delta, δ , or DOP (for delta opioid peptide); kappa, κ, or KOP (for kappa opioid peptide); and NOP (for nociceptin opioid peptide) are considered interchangeable abbreviations. Distinct cDNA sequences have been cloned for all four opioid receptor types, and each type appears to have a unique distribution in the brain, spinal cord, and periphery (Smith and Lee, 2003).

The diversity of opioid receptors is further extended by the existence of several subtypes of μ , δ , and κ receptors.

Based on pharmacological studies, there are thought to be at least three μ receptor subtypes, $\mu_1,\,\mu_2,$ and $\mu_3;$ two δ receptor subtypes, δ_1 and $\delta_2;$ and perhaps as many as four κ receptor subtypes, $\kappa_{1a},\,\kappa_{1b},\,\kappa_2,$ and κ_3 (Smith and Lee, 2003). The discovery of opioid receptor subtypes generated great enthusiasm among researchers and introduced the possibility of developing subtype-specific therapeutic agents with favorable side-effect profiles. At this point, however, the functional significance of these receptor subtypes remains unclear and distinct cDNA sequences corresponding to these subtypes have not yet been identified (Smith and Lee, 2003).

In general, it appears that the μ receptor mediates most of the clinically relevant analgesic effects, as well as most of the adverse side effects associated with opioid administration (Kieffer, 1999). Drugs acting at the $\boldsymbol{\delta}$ receptor tend to be poor analgesics, but may modify μ receptor-mediated antinociception under certain circumstances and mediate opioid receptor "cross-talk." The κ receptor mediates analgesia in several specific locations in the CNS and the periphery; however, distinguishing μ and κ-mediated analgesic effects has proved to be difficult (Kieffer, 1999; Smith and Lee, 2003). In contrast to the classic opioid receptors, the nociceptin receptor does not mediate typical opioid analgesia, but instead produces anti-opioid (pro-nociceptive) effects (Moran, Abdulla, and Smith, 2000, 2001; Janecka, Fichna, and Janecki, 2004). Because of the considerable structural homology among the three classically described opioid receptors, it is likely that there are significant interactions among these receptors in different tissues, and the loosely defined physiological roles ascribed to each receptor type still require further clarification.

Endogenous Opioid Receptor Ligands

The opioid receptors discussed in the preceding are part of an extensive opioid system that includes a large number of endogenous opioid peptide ligands. Endogenous opioid peptides are small molecules that are naturally produced in the CNS and various glands throughout the body, such as the pituitary and adrenal (Janecka, Fichna, and Janecki, 2004). Three classical families of endogenous opioid peptides have been identified: the enkephalins, dynorphins, and β -endorphin. Each of these is derived from a distinct precursor polypeptide, pro-enkephalin, pro-dynorphin, and proopiomelanocortin, respectively (Janecka, Fichna, and Janecki, 2004). These classical endogenous opioid peptides are expressed throughout the CNS, and their presence has more recently been confirmed in peripheral tissues as well (Janecka, Fichna, and Janecki, 2004). There are considerable structural similarities among these three groups of peptides, and each family demonstrates variable affinities for μ , δ , and κ receptors. None of them binds exclusively to a single opioid receptor and

none of them has any significant affinity for the nociceptin receptor. The physiological roles of these peptides are not completely understood at this time. They appear to function as neurotransmitters, neuromodulators and, in some cases, neurohormones. They mediate some forms of stress-induced analgesia and also play a role in analgesia induced by electrical stimulation of discrete regions in the brain, such as the periaqueductal gray of the mesencephalon (Inturrisi, 2002).

Nociceptin (orphanin FQ) is the endogenous ligand for the more recently discovered nociceptin-receptor. Nociceptin is derived from pro-nociceptin, and its amino acid sequence is closely related to that of the classical endogenous opioid peptides discussed above (Moran, Abdulla, and Smith, 2000; Janecka, Fichna, and Janecki, 2004). Despite this homology, nociceptin binding is specific for the nociceptin-receptor and the peptide does not appear to interact with μ , δ , or κ receptors. Furthermore, the physiological effects of nociceptin are in direct contrast to the actions of the classical endogenous opioid peptides, with nociceptin producing a distinctly pro-nociceptive effect (Moran, Abdulla, and Smith, 2000; Smith and Moran, 2001; Janecka, Fichna, and Janecki, 2004). The functional significance of nociceptin and its receptor remain to be elucidated, but additional insight into this novel opioid peptide may have substantial implications in future therapeutic drug development.

In addition to the enkephalins, dynorphins, β -endorphin and nociceptin, there are now two other recently discovered endogenous opioid peptides called endomorphin-1 and endomorphin-2 (Zadina et al., 1999). These peptides are putative products of an, as yet, unidentified precursor and have been proposed to be the highly selective endogenous ligands for the μ receptor (Zadina et al., 1999; Janecka, Fichna, and Janecki, 2004). The endomorphins are small tetrapeptides that are structurally unrelated to the classical endogenous opioid peptides (Zadina et al., 1999). Their identification has heralded a new era in research of the μ opioid system that may contribute to our understanding of the neurobiology of opioids, and provide new avenues for therapeutic interventions.

Opioid Receptor Signaling and Mechanisms of Analgesia

Binding of an opioid agonist to a neuronal opioid receptor, regardless of whether the agonist is endogenous or exogenous, typically leads to several events that serve to inhibit the activation of the neuron. Opioid receptors are part of a large superfamily of membrane-bound receptors that are coupled to G-proteins (Smith and Lee, 2003). As such, they are structurally and functionally related to receptors for many neurotransmitters and other neuropeptides that act to modulate the activity of nerve cells. Opioid receptor binding, via activation of various types of G-proteins, may lead to inhibition

of adenylyl cyclase (cyclic adenosine monophosphate [cAMP]) activity, activation of receptor-operated K^+ currents, and suppression of voltage-gated Ca^{2+} currents (Inturrisi, 2002).

At the pre-synaptic level, decreased Ca2+ influx results in reduced release of transmitter substances, such as substance P, from primary afferent fibers in the spinal cord dorsal horn, thereby inhibiting synaptic transmission of nociceptive input (Inturrisi, 2002). Postsynaptically, enhanced K⁺ efflux results in neuronal hyperpolarization of spinal cord projection neurons and inhibition of ascending nociceptive pathways. A third potential mode of opioid action involves upregulation of supraspinal descending antinociceptive pathways in the periaqueductal gray. It is now known that this system is subject to tonic inhibition mediated by GABAergic neurons, and opioid receptor activation has been shown to suppress this inhibitory influence and augment descending antinociceptive transmission (Christie, Connor, and Vaughan, 2000; Inturrisi, 2002). The proposed cellular basis for this involves μ receptors present on pre-synaptic GABAergic nerve terminals that activate voltage-dependent K⁺ currents and thereby inhibit GABA release into the synaptic cleft (Christie, Connor, and Vaughan, 2000). It is important to note that although our collective understanding of opioid receptor-mediated signaling has increased dramatically in recent years, the relationship of such subcellular events to clinical analgesia at the level of the organism requires further clarification.

Opioid Receptor Distribution and Therapeutic Implications

Although cellular and molecular studies of opioid receptors and ligands are invaluable in understanding their function, it is critical to place them in their anatomical and physiological context to fully appreciate the opioid system and its relevance to pain management. It has long been a principal tenet of opioid analgesia that these agents are centrally acting, and this understanding has shaped the way we use opioid analgesics clinically. It has been well established that the analgesic effects of opioids arise from their ability to directly inhibit the ascending transmission of nociceptive information from the spinal cord dorsal horn, and activate pain control circuits that descend from the midbrain via the rostral ventromedial medulla to the spinal cord. Within the CNS, evidence of μ , δ , and κ opioid receptor mRNA and/or opioid peptide binding has been demonstrated in supraspinal sites, including the mesencephalic periaqueductal gray, the mesencephalic reticular formation, various nuclei of the rostral ventromedial medulla, forebrain regions including the nucleus accumbens, as well as spinally within the dorsal horn (Yaksh, 1998; Gutstein and Akil, 2001). The interactions between groups of opioid receptors at various spinal and supraspinal locations, as well as

interactions between different receptor types within a given location are complex and incompletely understood at this time.

Systemic administration of opioid analgesics via IV, IM, or subcutaneous injection results in a relatively rapid onset of action via interaction with these CNS receptors. Oral, transdermal, rectal, or buccal mucosal administration of opioids results in variable systemic absorption, depending on the characteristics of the particular agent, with analgesic effects being mediated largely by the same receptors within the CNS. In addition, neuraxial administration, either into the subarachnoid or epidural space, is a particularly efficacious route of administration. Small doses of opioids introduced via these routes readily penetrate the spinal cord and interact with spinal and/or supraspinal opioid receptors to produce profound and potentially longlasting analgesia, the characteristics of which depend on the particular drug used.

Despite the fact that opioids have long been considered the prototype of centrally acting analgesics, a body of evidence has emerged over the past decade that clearly indicates that opioids can produce potent and clinically measurable analgesia by activation of opioid receptors in the peripheral nervous system (Stein, Machelska, and Schafer, 2001). Opioid receptors of all three major types have been identified on the processes of sensory neurons, and they respond to peripherally applied opioids and locally released endogenous opioid peptides when upregulated during inflammatory pain states (Fields et al., 1980; Stein, Hassan, and Lehrberger, 1993a; Stein, 1993b; Stein, Machelska, and Schafer 2001; Stein, Schafer, and Machelska, 2003). Furthermore, sympathetic neurons and immune cells also have been shown to express opioid receptors, but their functional role remains unclear (Stein, Schafer, and Machelska, 2003). Although the binding characteristics of peripheral and central opioid receptors are similar, the molecular mass of peripheral and central μ opioid receptors appears to be different, suggesting that selective ligands for these peripheral receptors could be developed that would produce opioid analgesia without the potential to induce centrally mediated adverse side effects (Stein, 1995; Stein, Pfluger, and Yassouridis, 1996; Stein and Yassouridis, 1997; Stein, Machelska, and Schafer, 2001; Stein, Schafer, and Machelska, 2003).

Adverse Effects of Clinically Used Opioids

Although opioids are used clinically primarily for their pain-relieving properties, they also produce a host of other effects on a variety of body systems. This is not surprising in light of the wide distribution of endogenous opioid peptides and their receptors in supraspinal, spinal, and peripheral locations. Because information regarding opioid side effects in most wild and exotic animals is lacking, reference is made to common domestic species where appropriate.

Central Nervous System

Level of Arousal There are considerable species differences in the CNS response to opioid analgesics that cannot be attributed to pharmacokinetic variations alone. CNS depression (i.e., sedation) is typically seen in the dog, monkey, and human, whereas CNS stimulation (i.e., excitement and/or spontaneous locomotor activity) may be elicited in the cat, horse, goat, sheep, pig, and cow following systemic administration of various opioids, most notably morphine (Branson, Gross, and Booth, 2001). Reasons for these different responses are not entirely clear at this time, but are presumably related to differing concentrations and distributions of μ , δ , and δ receptors in various regions of the brain in these species (Hellyer, Bai, and Supon, 2003). Details regarding the CNS responses of specific wild and exotic species to opioids are not known at this time. Regardless of the species, however, numerous factors may play a role, including the temperament or condition of the animal; the presence or absence of pain in the animal; the dose, route, and timing of drug administration; and the specific opioid administered.

Thermoregulatory Center The hypothalamic thermoregulatory system is also affected by opioid administration. Hypothermia tends to be the most common response, particularly when opioids are used during the perioperative period in the presence of other CNS depressant drugs (Branson, Gross, and Booth, 2001; Gutstein and Akil, 2001). Under some clinical circumstances, however, hyperthermia is observed in cats, horses, swine, and ruminants following opioid administration. Part of this increase in body temperature may be attributed to an increase in muscle activity associated with CNS excitation in these species; however, a specific central hypothalamic mechanism also has been implicated but remains poorly understood (Branson, Gross, and Booth, 2001).

Emetic Center Nausea and vomiting associated with opioid administration are a result of direct stimulation of the chemoreceptor trigger zone for emesis located in the area postrema of the medulla (Stoelting, 1999; Gutstein and Akil, 2001). As with the other centrally mediated side effects, species plays a role in determining an individual's tendency to vomit after an opioid is administered. Horses, rabbits, ruminants, and swine do not vomit with opioid administration. Cats may vomit, but usually at doses that are greater than those that stimulate vomiting in dogs. Dogs commonly vomit following opioid administration, especially with morphine.

Cough Center Opioids have variable efficacy in depressing the cough reflex, at least in part by a direct effect on a cough center located in the medulla (Gutstein and Akil, 2001). Certain opioids are more effective

antitussives than others, including drugs such as codeine, hydrocodone, and butorphanol.

Pupillary Diameter As a general rule, opioids tend to produce mydriasis in those species that exhibit CNS excitation, and miosis in those that become sedated following opioid administration (Lee and Wang, 1975; Wallenstein and Wang, 1979; Branson, Gross, and Booth, 2001; Stephan et al., 2003). Miosis is caused by an excitatory action of opioids on neuronal firing in the oculomotor nucleus (Lee and Wang, 1975; Wallenstein and Wang, 1979; Stoelting, 1999). In the cat, and presumably in other species that exhibit mydriasis, this increase in activity in the oculomotor nuclear complex still occurs, but the miotic effect is masked by increased release of catecholamines, which results in mydriasis (Wallenstein and Wang, 1979).

Respiratory System Opioids produce dose-dependent depression of ventilation, primarily mediated by μ_2 receptors leading to a direct depressant effect on brainstem respiratory centers (Stoelting, 1999; Gutstein and Akil, 2001). This effect is characterized by decreased responsiveness of these centers to carbon dioxide and is reflected in an increased resting PaCO₂ and displacement of the carbon dioxide response curve to the right. This effect is compounded by the co-administration of sedative and/or anesthetic agents, meaning that significant respiratory depression and hypercapnia are much more likely to occur in anesthetized patients that receive opioids versus those that are conscious. It should be noted that, in general, humans tend to be more sensitive to the respiratory depressant effects of opioids when compared with most veterinary species.

Cardiovascular System Most opioids have minimal effects on cardiac output, cardiac rhythm, and arterial blood pressure when clinically relevant analgesic doses are administered. Bradycardia may occur as a result of opioid-induced medullary vagal stimulation and responds readily to anticholinergic treatment if warranted. Particular opioids (morphine and meperidine) can cause release of histamine, especially after rapid IV administration, which may lead to vasodilation and hypotension (Branson, Gross, and Booth, 2001; Smith et al., 2001). Because of their relatively benign effects on cardiovascular function, opioids commonly form the basis of anesthetic protocols for human patients or animals with preexisting cardiovascular disease.

Gastrointestinal System The gastrointestinal effects of the opioids are mediated by μ and δ receptors located in the myenteric plexus of the gastrointestinal tract (Branson, Gross, and Booth, 2001; Gutstein and Akil, 2001). Opioid administration may stimulate defecation in certain species. Following this initial response, spasm of gastrointestinal smooth muscle predisposes to ileus

and constipation. Horses and ruminants in particular may be predisposed to gastrointestinal complications associated with opioid administration such as colic and ruminal tympany, respectively. Chronic opioid use may predispose to gastrointestinal stasis in other species.

In human patients, opioids (most notably fentanyl and morphine) have been shown to increase bile duct pressure through constriction of the sphincter of Oddi (Radnay et al., 1984). The incidence of this side effect in humans, however, is quite low (Jones, Detmer, and Hill, 1981). The incidence of increased bile duct pressure secondary to opioid administration in various animal species, and its potential clinical significance, are unknown at this time.

Genitourinary System Opioids, particularly when administered neuraxially, may cause urinary retention through dose-dependent suppression of detrusor contractility and decreased sensation of urge (el Bindary and Abu el-Nasr, 2001; Kuipers et al., 2004). Urine volume also may be affected by opioids, and the mechanism of this effect appears to be multifactorial. μ Agonists tend to produce oliguria in the clinical setting, and this is in part a result of increased antidiuretic hormone release leading to altered renal tubular function (Stoelting, 1999; Mercadante and Arcuri, 2004). Elevations in circulating plasma atrial natriuretic peptide may also play a role in morphine-induced antidiuresis (Mercadante and Arcuri, 2004). Conversely, к agonists tend to produce a diuretic effect, possibly through inhibition of antidiuretic hormone secretion (Stoelting, 1999; Mercadante and Arcuri, 2004). Other peripheral mechanisms involving stimulation of renal α_2 adrenergic receptors may also contribute to this к agonist effect (Mercadante and Arcuri, 2004).

Opioid Agonists

Almost all clinically useful opioids exert their analgesic effects by acting as agonists at μ receptors. Although there are a few opioids that act as k agonists, these drugs also tend to have antagonist or partial agonist effects at μ and/or δ receptors, and thus are not classified as *pure* agonists. Pure or full opioid agonists are capable of eliciting maximal activation of the receptor when they bind it and the subsequent downstream processes result in a maximal analgesic effect (Figure 1.1). Clinically the full μ agonists are superior analgesics, and they are the drugs of choice for pain of moderate to severe intensity in many veterinary species. The following section contains brief descriptions of full μ agonists currently used in veterinary medicine. Specific details regarding μ agonist clinical pharmacology in various wild and exotic species is lacking.

Morphine (Morphine Sulfate) Morphine is the prototypical opioid analgesic and acts as a full agonist not

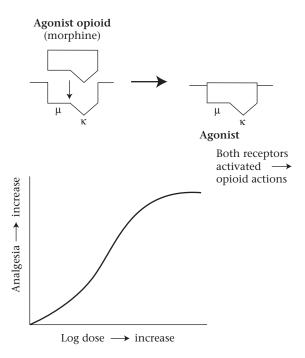


Figure 1.1. Effects of opioid agonists.

only at μ receptors, but also at δ and κ receptors (Gutstein and Akil, 2001). Despite the development of numerous synthetic opioids, many of which are more potent than morphine and may have other characteristics that make them desirable alternatives to morphine in certain circumstances, it is worth noting that no other drug has been shown to be more efficacious than morphine at relieving pain in humans. Compared with the synthetic opioid agonists, morphine is relatively hydrophilic in nature and crosses the blood-brain barrier more slowly than fentanyl or oxymorphone, thereby delaying the peak effect somewhat even after IV administration (Stoelting, 1999; Gutstein and Akil, 2001). Clinically this lag is not likely to be significant under most circumstances, with the onset of analgesia occurring reasonably promptly after a single dose of morphine and typically lasting 3 to 4 hours (Barnhart, Hubbell, and Muir, 2000; Taylor et al., 2001). Morphine's poor lipid solubility means that it can produce longlasting analgesia when administered into the epidural or subarachnoid space, with effects persisting for 12 to 24 hours. The first-pass effect is significant after oral administration and the bioavailability of oral morphine preparations is only in the range of 25%.

In most species, the primary metabolic pathway for morphine involves conjugation with glucuronic acid leading to the formation of two major metabolites, morphine-6-glucuronide and morphine-3-glucuronide (Faura et al., 1998; Gutstein and Akil, 2001). Despite the low levels of glucuronyl transferase in the cat, the pharmacokinetics of morphine in this species seems to be broadly comparable to the dog and human, although clearance rates may be marginally slower (Faura et al.,

1998; Barnhart, Hubbell, and Muir, 2000; Taylor et al., 2001). This suggests that morphine must undergo a different type of conjugation reaction in this species. Morphine-6-glucuronide has pharmacological activities that are indistinguishable from those of morphine in animal models and human beings, whereas morphine-3-glucuronide appears to have little affinity for opioid receptors, but may contribute to the excitatory effects of morphine in some situations (Smith, 2000; Gutstein and Akil, 2001). With chronic morphine administration, it is likely that the active metabolite, morphine-6-glucuronide, contributes significantly to clinical analgesia.

Very little morphine is excreted unchanged in the urine. The major metabolites, morphine-3-glucuronide and, to a lesser extent, morphine-6-glucuronide, are eliminated almost entirely via glomerular filtration. In human patients, renal failure may lead to accumulation of morphine-6-glucuronide and persistent clinical effects, whereas liver dysfunction seems to have minimal impact on morphine clearance (Stoelting, 1999; Gutstein and Akil, 2001).

The side effects associated with morphine administration are typical of most opioid agonists and have been discussed previously in this chapter. In particular, the increased incidence of vomiting after morphine administration as well as its potential to cause histamine release after IV administration distinguish morphine from other full opioid agonists.

Oxymorphone Oxymorphone is a synthetic opioid that acts as a full agonist at μ receptors and is comparable to morphine in its analgesic efficacy and duration of action. It is a more lipid soluble drug than morphine and is readily absorbed after IM or subcutaneous administration. Oxymorphone is not available as an oral formulation.

When compared with morphine, oxymorphone may be less likely to cause vomiting and tends to produce more sedation when administered to domestic species. Its respiratory depressant effects are similar to those induced by morphine, but oxymorphone seems more likely to cause panting in dogs. It does not produce histamine release, even when administered intravenously (Smith et al., 2001). Oxymorphone's other side effects are typical of other full μ agonist opioids and have been discussed previously.

Hydromorphone Hydromorphone is a synthetic opioid that acts as a full agonist at μ receptors and is used in both human and veterinary medicine. Clinically, hydromorphone and oxymorphone have similar efficacy, potency, duration of analgesic action, and side effect profiles, but hydromorphone remains significantly less expensive. Like oxymorphone, hydromorphone is not associated with histamine release, so bolus IV administration is considered safe (Smith et al., 2001).

Meperidine Meperidine is a synthetic opioid that exerts its analgesic effects through agonism at μ receptors. Interestingly, it also appears able to bind to other types of receptors, which may contribute to some of its clinical effects other than analgesia. Meperidine is capable of blocking sodium channels and inhibiting activity in dorsal horn neurons in a manner analogous to local anesthetics (Wagner et al., 1999; Wolff et al., 2004). Also it has been shown recently that meperidine exerts agonist activity at α_2 receptors, specifically the α_{2B} subtype, suggesting that it may possess some α_2 agonist-like properties (Takada, Tonner, and Maze, 1999; Takada, Clark, and Davies, 2002).

Meperidine has a considerably shorter duration of analgesic action compared with morphine, oxymorphone, or hydromorphone, typically not extending beyond 1 hour (Branson, Gross, and Booth, 2001). Metabolic pathways vary among different species but, in general, most of the drug is demethylated to normeperidine in the liver and then undergoes further hydrolysis and ultimately renal excretion (Yeh, Krebs, and Changchit, 1981; Branson, Gross, and Booth, 2001; Taylor et al., 2001). Normeperidine is an active metabolite and possesses approximately one-half the analgesic efficacy of meperidine (Branson, Gross, and Booth, 2001; Gutstein and Akil, 2001). Normeperidine has produced toxic neurological side effects in human patients receiving meperidine for prolonged periods of time, especially in the presence of impaired renal function (Stone, Macintyre, and Jarvis, 1993; Stoelting, 1999).

Unlike most of the other opioids in clinical use, meperidine has been shown to produce significant negative inotropic effects when administered alone to conscious dogs (Priano and Vatner, 1981). As well, because of its modest atropine-like effects, meperidine tends to increase heart rate rather than predispose to bradycardia as is often seen with other opioids (Stoelting, 1999; Branson, Gross, and Booth, 2001). The clinical significance of these cardiovascular effects in the perianesthetic period has never been clearly ascertained. Like morphine, meperidine also causes histamine release when administered intravenously (Branson, Gross, and Booth, 2001).

A rare but life-threatening drug interaction has been reported in human patients receiving meperidine that may have relevance in veterinary medicine. The combination of meperidine (and perhaps other opioids) with a monoamine oxidase inhibitor (MAOI) may lead to serotonin syndrome, which is characterized by a constellation of symptoms, including confusion, fever, shivering, diaphoresis, ataxia, hyperreflexia, myoclonus, and diarrhea (Sporer, 1995; Bowdle, 1998; Heinonen and Myllyla, 1998; Tissot, 2003). An MAOI, selegiline (Deprenyl), has been used in dogs to treat pituitary-dependent hyperadrenocorticism or modify behavior in patients with canine cognitive dysfunction. Although to date there have not been any reports of

adverse meperidine–selegiline interactions in dogs, the veterinarian must be aware of the potential for complications if analgesia is required in patients receiving MAOIs. A recent study has evaluated the effects of other opioids (oxymorphone and butorphanol) in selegiline-treated dogs and did not identify any specific adverse drug interactions in these animals (Dodam et al., 2004).

Fentanyl Fentanyl is a highly lipid soluble, short-acting synthetic μ opioid agonist. A single dose of fentanyl administered intravenously has a more rapid onset and a shorter duration of action than morphine. Peak analgesic effects occur in about 5 minutes and last approximately 30 minutes (Stoelting, 1999; Gutstein and Akil, 2001). Rapid redistribution of the drug to inactive tissue sites, such as fat and skeletal muscle, leads to a decrease in plasma concentration and is responsible for the prompt termination of clinical effects. In most veterinary species the elimination half-time after a single bolus or a brief infusion is in the range of 2 to 3 hours (Carroll et al., 1999; Lee, Papich, and Hardie, 2000; Maxwell et al., 2003). Administration of very large doses or prolonged infusions may result in saturation of inactive tissues with termination of clinical effects becoming dependent on hepatic metabolism and renal excretion (Stoelting, 1999; Gutstein and Akil, 2001). Thus, the context-sensitive half-time of fentanyl increases significantly with the duration of the infusion, and clinical effects may persist for an extended period following termination of a long-term IV infusion.

Side effects associated with fentanyl administration are similar to those of the other full μ agonist opioids. In general, cardiovascular stability is excellent with fentanyl and IV administration is not associated with histamine release (Stoelting, 1999; Gutstein and Akil, 2001). Bradycardia may be significant with bolus doses but readily responds to anticholinergics if treatment is warranted (Branson, Gross, and Booth, 2001; Gutstein and Akil, 2001). In human patients muscle rigidity, especially of the chest wall, has been noted after administration of fentanyl or one of its congeners. The potential significance of this adverse effect in animal patients is not clear at this time, and the risk is considered minimal if large rapid bolus administrations are avoided.

Clinically, fentanyl is used most frequently in dogs and cats but it is also a potentially useful analgesic in other species, including the horse, cow, sheep, goat, and pig. Historically, fentanyl was available in combination with the butyrophenone tranquilizer, droperidol, in a product called Innovar-Vet, which was typically administered in the pre-anesthetic period to provide sedation and analgesia. This product is no longer available, and systemic administration of fentanyl today is usually via the IV route.

The development of novel less-invasive routes of opioid administration for use in human patients led to the

marketing of transdermal fentanyl patches (Duragesic). The patches are designed to release a constant amount of fentanyl per hour, which is then absorbed across the skin and taken up systemically. Fentanyl patches are designed for human skin and human body temperature; however, their use has been evaluated in a number of domestic veterinary species (Egger et al., 1998, 2003; Carroll et al., 1999; Robinson et al., 1999; Wilkinson, Thomas, and Morse, 2001; Gellasch et al., 2002; Maxwell et al., 2003; Gilberto, Motzel, and Das, 2003). Substantial variations in plasma drug concentrations have been documented and significant lag times after patch placement are common prior to onset of analgesia (Egger et al., 1998, 2003; Carroll et al., 1999; Lee, Papich, and Hardie, 2000). Furthermore, changes in body temperature have been shown to significantly affect fentanyl absorption in anesthetized cats, and it is likely that other factors associated with skin preparation and patch placement have the potential to substantially alter plasma fentanyl levels and analgesic efficacy (Pettifer and Hosgood, 2003). Fentanyl patch safety and efficacy in most species is unknown at this time.

Alfentanil, Sufentanil, and Remifentanil Alfentanil, sufentanil, and remifentanil are all structural analogues of fentanyl that were developed for use in humans in an effort to create analgesics with a more rapid onset of action and predictable termination of opioid effects. All three are similar with regard to onset and all have context-sensitive half-times that are shorter than that of fentanyl after prolonged infusions (Stoelting, 1999). Remifentanil is unique among opioids because it is metabolized by non-specific plasma esterases to inactive metabolites (Chism and Rickert, 1996; Hoke et al., 1997). Thus, hepatic or renal dysfunction has little impact on drug clearance and this, in combination with the robust nature of the esterase metabolic system, contributes to the predictability associated with infusion of remifentanil (Stoelting, 1999; Gutstein and Akil, 2001).

All three of these drugs are used during general anesthesia for procedures requiring intense analgesia and/or blunting of the sympathetic nervous system response to noxious stimulation. As yet, they have limited applications for postoperative or chronic pain management. Like fentanyl, they can be administered at relatively low infusion rates as adjuncts to general anesthetic protocols based on volatile inhalant or other injectable agents, or they can be administered at higher rates as the primary agent for total IV anesthesia. The minimum alveolar anesthetic concentration-sparing properties of these agents have been demonstrated in both the dog and cat (Michelsen et al., 1996; Hoke et al., 1997; Ilkiw, Pascoe, and Fisher, 1997; Pascoe, Ilkiw, and Fisher, 1997; Mendes and Selmo, 2003). In the horse, systemic infusions of alfentanil did not have significant effects on minimum alveolar concentrations of inhalant anesthetics and when administered to conscious horses were

associated with increases in locomotor activity (Pascoe et al., 1991; Pascoe and Taylor, 2003). There is little evidence to suggest that any of the fentanyl analogues offer advantages over morphine when administered into the epidural space for analgesia (Natalini abd Robinson, 2000).

Methadone Methadone is a synthetic μ opioid agonist with pharmacological properties qualitatively similar to those of morphine, but possessing additional affinity for NMDA receptors (Gorman, Elliott, and Inturrisi, 1997; Ripamonti and Dickerson, 2001). Methadone's unique clinical characteristics include excellent absorption following oral administration, no known active metabolites, high potency, and an extended duration of action (Branson, Gross, and Booth, 2001; Gutstein and Akil, 2001; Ripamonti and Dickerson, 2001). In human patients, the drug has been used primarily in the treatment of opioid abstinence syndromes, but is being used increasingly for the management of chronic pain. Although there are reports of IM or IV administration of methadone in the perioperative period in dogs, cats, and horses, the drug is not commonly used in this setting in North America at this time (Fisher, 1984; Dobromylskyj, 1996; Kramer, 1996).

Codeine Codeine is the result of substitution of a methyl group onto morphine, which acts to limit first-pass hepatic metabolism and accounts for codeine's high oral bioavailability (Stoelting, 1999; Gutstein and Akil, 2001). Codeine is well known for its excellent antitussive properties and is often combined in an oral formulation with a non-opioid analgesic, such as acetaminophen (Tylenol 3), for the management of mild to moderate pain in human patients.

Oxycodone and Hydrocodone Oxycodone and hydrocodone are opioids that are typically administered orally for the treatment of pain in human patients. Although oxycodone is available as a single drug continuous-release formulation (Oxycontin), these drugs are most often prepared in combination with non-opioid analgesics such as aspirin and acetaminophen (Percocet, Percodan, Lorcet, Vicodin, etc.). Little has been published regarding the use of these opioids in veterinary species.

Etorphine and Carfentanil (M-99 and Wildnil, Respectively) These two opioids are discussed together because they are both used exclusively for the restraint and capture of wild animals, rather than as analgesic agents. They are extremely potent opioids and the immediate availability of a suitable antagonist is mandatory before these drugs are to be used, not only to reverse drug effects in animal patients, but also as a safety precaution in the event of accidental human injection. Although etorphine and carfentanil are most

often injected intramuscularly (usually using a remote drug delivery technique), recent studies suggest that carfentanil is useful when administered orally in a variety of species, including the brown bear, Brazilian tapir, and chimpanzee (Kearns, Swenson, and Ramsay, 2000; Mama, Steffey, and Withrow, 2000; Mortenson and Bechert, 2001; Pollock and Ramsay, 2003). A number of different drugs have been used in combination with etorphine or carfentanil to enhance muscle relaxation, including acepromazine, xylazine, and medetomidine (Caulkett, Cribb, and Haigh, 2000; Ramdohr et al., 2001; Roffe, Coffin, and Berger, 2001; Miller et al., 2003).

Opioid Agonist-Antagonists and Partial Agonists

This group includes drugs that have varying opioid receptor binding profiles, but that have one thing in common: They all occupy μ opioid receptors, but do not initiate a maximal clinical response. Drugs such as butorphanol and nalbuphine are classified as agonistantagonists. They are competitive µ receptor antagonists, but exert their analgesic actions by acting as agonists at κ receptors (Figure 1.2). Buprenorphine, on the other hand, is classified as a partial agonist and binds μ receptors but produces only a limited clinical effect (Figure 1.3). These mixed agonist-antagonist drugs were developed for the human market in an attempt to create analgesics with less respiratory depression and addictive potential. Because of their opioid receptor binding affinities, the side effects associated with these drugs demonstrate a so-called "ceiling effect," whereby increasing doses do not produce additional adverse responses. Unfortunately, the benefits of this ceiling effect on ventilatory depression come at the expense of limited analgesic efficacy and only a modest ability to decrease anesthetic requirements.

The co-administration of opioids with differing receptor binding profiles is currently an active area of research that deserves further attention. The interactions in this setting are complex and it appears that opioid co-administration has the potential to produce additive, synergistic, or antagonistic analgesic effects depending on the particular species, dosage, drugs, and pain model being evaluated. The following section contains brief descriptions of opioid agonist-antagonists and partial agonists that are currently used in veterinary medicine.

Butorphanol Butorphanol is a synthetic agonist-antagonist opioid and has been used extensively in a wide variety of veterinary species. The drug was originally labeled as an antitussive agent in dogs and, even now, is approved as an analgesic in the cat and horse only (Branson, Gross, and Booth, 2001). Butorphanol exerts its relevant clinical effects through its interactions at κ receptors and acts as an antagonist at μ receptors. The duration of butorphanol's analgesic effects remains somewhat debatable and likely varies with species, type and intensity of pain, dosage, and route of administration (Sawyer et al., 1991; Sellon et al., 2001; Robertson, Taylor, and Lear, 2003). In general, its effects are shorter lived than those of morphine and are probably in

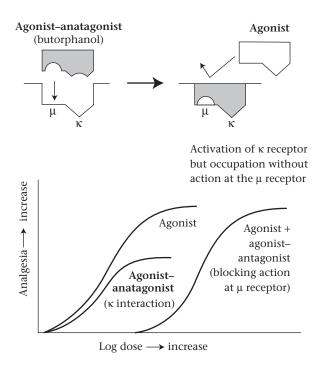


Figure 1.2. Activation of κ receptor, but occupation without action at the μ receptor.

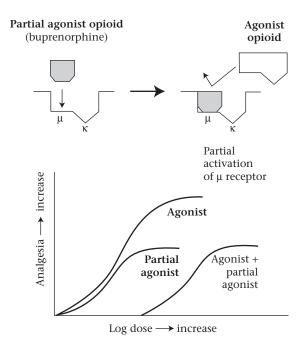


Figure 1.3. Partial activation of μ receptor.

the range of 1 to 3 hours. Butorphanol does not induce histamine release when administered intravenously and has minimal effects on cardiopulmonary function. There is conflicting evidence regarding the effects of butorphanol on inhalant anesthetic requirements in the dog, cat, and horse. Earlier studies failed to demonstrate a significant sparing effect on minimum alveolar concentration when butorphanol was co-administered with halothane in dogs and ponies (Matthews and Lindsay, 1990; Quandt, Raffe, and Robinson, 1994; Doherty, Geiser, and Rohrbach, 1997). More recently, isoflurane MAC reductions have been documented after administration of clinically relevant doses of butorphanol in both dogs and cats. Reasons for these discrepancies are probably related to differences in study techniques and, in the dog and cat specifically, it seems that butorphanol is capable of inducing at least modest reductions in inhalant anesthetic requirements.

Traditionally, it was thought that the simultaneous or sequential administration of butorphanol with a pure μ opioid agonist such as morphine or hydromorphone would be counterproductive from an analgesic standpoint because butorphanol's ability to antagonize µ receptors could inhibit or even reverse the effects of the agonist drug. Certainly, it has been clearly demonstrated that excessive sedation associated with a pure μ agonist can be partially reversed by the administration of low doses of butorphanol, and it was presumed that butorphanol would similarly reverse the µ-mediated analgesic effects as well. It now appears that the potential interactions between but or phanol and full μ opioid agonists are more complex than originally believed. One study demonstrated that coadministration of butorphanol and oxymorphone to cats subjected to a visceral noxious stimulus resulted in enhanced analgesic effects (Briggs, Sneed, and Sawyer, 1998). A more recent feline study, however, evaluated the combination of butorphanol and hydromorphone in a thermal threshold pain model and failed to demonstrate enhanced analgesia. It suggested that butorphanol did, in fact, inhibit hydromorphone's analgesic effects (Lascelles and Robertson, 2004). These contradictory findings illustrate that we still have much to learn about co-administration of opioid agents with differing receptor binding profiles. The clinical effects produced by such co-administration likely depend on many factors, including species, type of pain, dose, and specific drugs involved.

Nalbuphine and Pentazocine Nalbuphine and pentazocine are classified as agonist-antagonist opioids and are clinically similar to butorphanol. They induce mild analgesia accompanied by minimal sedation, respiratory depression, or adverse cardiovascular effects. Like butorphanol, nalbuphine is occasionally used to partially reverse the effects of a full μ agonist opioid while maintaining some residual analgesia.

Buprenorphine Buprenorphine is a semisynthetic, highly lipophilic opioid derived from thebaine. Unlike other opioids in this category, buprenorphine is considered to be a partial agonist at μ opioid receptors. The drug binds avidly to and dissociates slowly from μ receptors, but is not capable of eliciting a maximal clinical response. Because of its receptor binding characteristics, buprenorphine has a delayed onset of action and takes at least 60 minutes to attain peak effect after IM administration. It also has a relatively long duration of action with clinical analgesic effects persisting for 6 to 12 hours in most species. Also, its high affinity for the μ receptor means that it may be difficult to antagonize its effects with a drug such as naloxone. Buprenorphine has most often been administered intravenously or intramuscularly; however, because of the long lag time before clinical effects are achieved after IM administration, the IV route is preferred. A recent study documented comparable plasma drug levels and analgesic efficacy with oral transmucosal administration in cats (Robertson et al., 2003).

Opioid Antagonists

These drugs have high affinities for the opioid receptors and are able to displace opioid agonists from μ and κ receptors. After this displacement, the pure antagonists bind to and occupy opioid receptors, but do not activate them (Figure 1.4). Under ordinary circumstances, in patients that have not received exogenous agonist opioids, the opioid antagonists have few clinical effects when administered at clinically relevant dosages (Gutstein and Akil, 2001). It is important to recognize

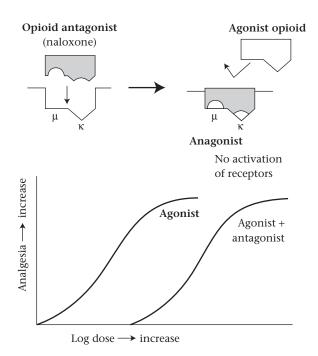


Figure 1.4. No activation of receptors.

that these drugs rapidly reverse all opioid-induced clinical effects, including analgesia.

Naloxone This pure opioid antagonist is capable of reversing all opioid agonist effects, producing increased alertness, responsiveness, coordination and, potentially, increased perception of pain. Naloxone's duration of action is shorter than many of the opioid agonists, with recommended IV doses lasting between 30 and 60 minutes. Consequently, animals need to be closely monitored for renarcotization after a dose of naloxone. Occasionally, excitement or anxiety may be seen after naloxone reversal of an opioid agonist. Premature ventricular contractions also have been documented after reversal, but are not a common occurrence and seem to be more likely if there are high levels of circulating catecholamines. This drug is sometimes administered sublingually to neonatal patients exhibiting respiratory depression that have been delivered by Caesarian section after maternal administration of an opioid agonist.

Nalmefene and Naltrexone Both of these drugs are pure opioid antagonists with clinical effects that last approximately twice as long as naloxone (Veng-Pedersen et al., 1995). Although little is published about the use of these drugs in veterinary patients, they may be advantageous in preventing renarcotization when used to antagonize the effects of a long-acting opioid.

NON-STEROIDAL ANTIINFLAMMATORIES

The NSAIDs relieve mild to moderately severe pain and have been used extensively in a wide variety of domestic animals for many years. Although pharmacokinetic and pharmacodynamic studies involving NSAIDs in wild and exotic animals are lacking, their use in such species continues to increase.

This class of drugs dates back thousands of years, with the salicylates being among the oldest and still most commonly used analgesics (Vane and Botting, 2003). Salicylate is a naturally occurring substance found in willow bark and was used for centuries to manage pain associated with rheumatism prior to production of the synthetic compound. In 1878, Felix Hoffman, working at the Bayer Company in Germany, made the acetylated form of salicylic acid that has come to be known as aspirin (Vane and Botting, 2003). Although aspirin (acetylsalicylic acid or ASA) has been found to be effective in the management of acute and chronic mild discomfort, the newer injectable NSAIDs appear to have comparable efficacy to the pure μ agonist opioids in controlling moderate to severe soft-tissue and orthopedic pain. The NSAIDs appear to confer synergism when used in combination with opioids and may demonstrate an opioid-sparing effect should lower dosages of opioid be required. Their extended duration of action in addition to their analgesic efficacy make the NSAIDs ideal for treating acute and chronic pain in veterinary species. Careful patient and drug selection is critical, however, because of their potential for harmful side effects.

The Cyclooxygenases and Prostaglandin Synthesis

In 1971, Vane discovered the mechanism by which aspirin exerts its antiinflammatory, analgesic, and antipyretic actions. He proved that aspirin and other NSAIDs inhibited the activity of a cyclooxygenase (COX) enzyme that produced prostaglandins (PGs) involved in the pathogenesis of inflammation, swelling, pain, and fever (Vane, 1971). Twenty years later, the discovery of a second COX enzyme was made, and more recently, a newly identified COX-3 (Botting, 2000; Chandrasekharan et al., 2002; Botting, 2003). Cyclooxygenase (previously termed prostaglandin synthase) oxidizes arachidonic acid (previously termed icosatetraenoic acid) to various eicosanoids (including PGs and other related compounds) (Figure 1.5) (Livingston, 2000). Oxidation of arachidonic acid by 5-lipoxygenase (5-LOX), the most biologically important of the mammalian oxygenases, results in the series of eicosanoids termed leukotrienes (Figure 1.5). The release of arachidonic acid from membrane phospholipid is catalyzed by the enzyme phospholipase A₂ and is the rate-limiting step in PG and leukotriene synthesis. Prostaglandin G₂ is the initial prostanoid formed, followed by prostaglandin H₂, which serves as a substrate for prostaglandin E-synthetase, prostaglandin D-isomerase, prostaglandin F-reductase, prostacyclin synthetase, and thromboxane synthetase for conversion to a variety of other prostanoids ubiquitous throughout cells and tissues in the body (Livingston, 2000). These include the PGs PGE₂, PGD₂, PGF₂, and PGI₂ (prostacyclin), and the thromboxanes TXA₂ and TXB₂, all with diverse functions (Vane and Botting, 1995) The PGs are not stored but are synthesized at a constant rate. They have short half-lives of 4 to 6 minutes at 37°C, and act locally at the site of production.

The PGs produced by both COX-1 and COX-2 are ubiquitous throughout the body and serve to facilitate many normal physiological functions during both health and illness. Consequently, the clinical use of NSAIDs has the potential to disrupt these functions with the possibility of significant organ dysfunction. Thus, in addition to their role as analgesics, the effects of NSAIDs on the constitutive functions of the PGs always must be considered. There are several key points to note: (1) COX-1 generates PGs that are responsible for mucosal defense (i.e., secretion of bicarbonate and mucus, mucosal blood vessel attenuation of constriction, and mucosal epithelial regeneration), as well as thromboxane A2, which is necessary for platelet function. (2) COX-2 produces PGs, which function in the prevention and promotion of healing of mucosal erosions,

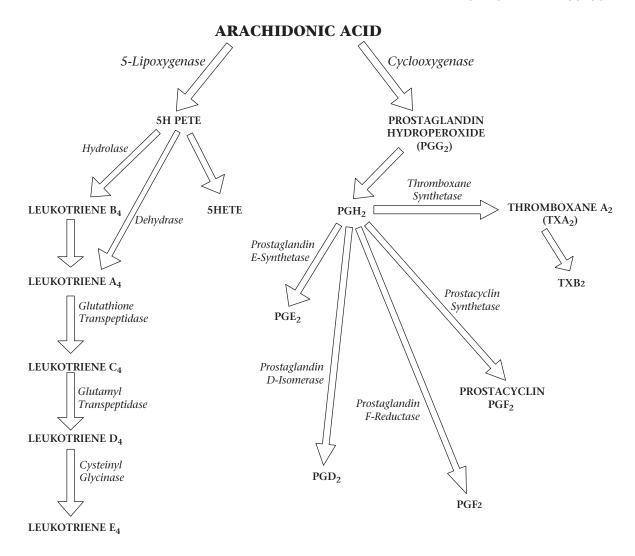


Figure 1.5. Eicosanoid synthesis.

exert antiinflammatory effects by inhibiting leukocyte adherence, as well as play a role in renal protection and maturation. (3) COX-3 produces PGs, which exert a protective function by initiating fever (Vane and Botting, 1995; Botting, 2003).

Thus, depending on the NSAID selected, primary plug formation of platelets, modulation of vascular tone in the kidney and gastric mucosa, cytoprotective functions within the gastric mucosa, smooth muscle contraction, and regulation of body temperature will all be affected (Vane and Botting, 1995). However, in this regard not all NSAIDs are created equal. As noted, the COX-1, COX-2, and COX-3 enzymes make variable contributions to these functions, and individual NSAIDs inhibit each of these enzymes differently. Some NSAIDs inhibit both COX-1 and COX-2 (i.e., aspirin, phenylbutazone, ketoprofen/Anafen, ketorolac/Toradol, flunixin meglumine/Banamine); other NSAIDs preferentially inhibit COX-2 with only weak inhibition of COX-1 (i.e., meloxicam/Metacam, carprofen/Rimadyl, etodolac/

Etogesic, vedaprofen/Quadrisol-5, tolfenamic acid/Tolfedine); and others inhibit COX-2 exclusively (i.e., Deracoxib/Deramax); whereas still another drug, acetaminophen, only weakly inhibits both COX-1 and COX-2, but is able to inhibit COX-3 activity preferentially (Botting, 2000).

Several in vitro studies investigating NSAID-selective inhibition of the COX-1 and COX-2 isoenzymes have been published; however, these are very difficult to interpret because of inconsistencies in the assays used (Kay-Mugford et al., 2000). Clinically this information is confusing as it does not consider the pharmacokinetics of particular drugs and their concentrations in various tissues (Bertolini et al., 2001). Most NSAIDs that inhibit COX have been shown to result in diversion of arachidonate to the 5-LOX pathway. The 5-LOX is principally found in polymorphonuclear cells, mast cells, monocytes, basophils, and B lymphocytes that are recruited during inflammatory and immune reactions (Bertolini et al., 2001). This enzyme catalyzes the initial step in

leukotriene biosynthesis, which subsequently produces various eicosanoids, with LTB_4 being the most notable potent mediator of inflammation. The excessive production of leukotrienes has been implicated in the creation of NSAID-induced ulcers (Rainsford, 1992; Hudson et al., 1993). As always, however, the biological system is not clear-cut. Although the LOX pathway is pro-inflammatory, there is also an antiinflammatory pathway, which is discussed in more detail later (Serhan and Chiang, 2004).

The contribution of the leukotrienes to the inflammatory process seems to suggest that inhibition of both the COX and 5-LOX pathways by a therapeutic agent would result in an enhanced safety profile and may confer even greater analgesic efficacy because of broader antiinflammatory and anti-nociceptive effects (Kirchner et al., 1997). Available data show that dual-acting compounds are effective in arthritic models, in which they also retain anti-thrombotic activity, produce little or no gastrointestinal damage, and do not adversely affect the asthmatic state (Bertolini et al., 2001). A recently approved dual COX/5-LOX inhibitor (tepoxalin/Zubrin) has undergone clinical trials and is now approved for veterinary use (Argentieri et al., 1994; Kirchner et al., 1997). Tepoxalin has demonstrated gastrointestinal antiinflammatory activity in mice, supporting the theory that 5-LOX inhibition has the potential to play a vital role in the prevention of NSAID-induced gastric inflammation (Kirchner et al., 1997).

The NSAIDs and Mechanisms of Analgesia

Prostaglandins, notably PGE_2 and prostacyclin, are potent mediators of inflammation and pain. These molecules exert hyperalgesic effects and enhance nociception produced by other mediators, such as bradykinin. The NSAIDs' analgesic mechanism of action is through inhibition of COX-1, COX-2, and COX-3 activity with subsequent prevention of PG synthesis.

The anti-nociceptive effects of the NSAIDs are exerted both peripherally and centrally (Chopra et al., 2000). The NSAIDS penetrate inflamed tissues, where they have a local effect, which makes them excellent analgesic choices for injuries with associated inflammation, as well as conditions such as synovitis, arthritis, cystitis, and dermatitis (Chopra et al., 2000). The central action is at both the spinal and supraspinal levels, with contributions from both COX-1 and COX-2 (Malmberg and Yaksh, 1992; McCormack, 1994; Yaksh et al., 1998; Chopra et al., 2000). This central effect may account for the overall well-being and improved appetite that is often observed in patients receiving parenterally administered NSAIDs for relief of acute pain.

The rational use of NSAIDs as analgesics should be based on an understanding of pain physiology and pathophysiology. Nociceptive pathways may involve either the COX-1 or COX-2 gene, and these genes are expressed in different locations and under different

circumstances. The COX-2 isoenzyme is known as the inducible isoform because it is upregulated in inflammatory states and is known to play a key role in nociception. Although the COX-1 gene has traditionally been thought of as being expressed constitutively, this isoenzyme also plays an integral role in the pain experience (Chandrasekharan et al., 2002). The COX-1 selective NSAIDs are superior to COX-2 selective NSAIDs at inhibiting visceronociception caused by chemical pain stimulators in a mouse peritoneal model (Ochi et al., 2000). This has been confirmed by visceronociception being greatly reduced in COX-1 but not COX-2 knockout mice (Ballou et al., 2000). These studies concluded that peripheral COX-1 mediates nociception in slowly developing pain in mice, such as in visceral pain, and central COX-1 may be involved in rapidly transmitted, non-visceral pain, such as that caused by thermal stimulation (Ballou et al., 2000). Visceral pain may be mediated, at least in part, by stimulation of intraperitoneal receptors located on sensory fibers by COX-1 produced prostacyclin (Botting, 2003). Interestingly, there may be gender differences as in Ballou's mouse model, which demonstrated that spinal COX-2 did in fact contribute to visceral nociception, but only in female mice (Ballou et al., 2000). The analgesic potency of a range of NSAIDs in relieving tooth-extraction pain in humans correlates closely with increasing selectivity toward COX-1 rather than COX-2. These findings highlight the importance of both COX-1 and COX-2 contributions to pain and the selective efficacy of the NSAIDs in treating various painful conditions.

The COX-2 or inducible isoenzyme can potentially increase by 20-fold over baseline in the presence of tissue injury and inflammation (Malmberg and Yaksh, 1992). Pro-inflammatory cytokines and mitogens such as interleukin-1-beta, (IL- β), interferon- γ , and tumor necrosis factor- α (TNF- α) induce COX-2 expression in macrophages, as can platelet-activating factor (PAF) and PGE₂ (Bertolini et al., 2001). These events also may occur in chondrocytes, osteoblasts, and synovial microvessel endothelial cells. The higher COX levels increase prostanoid production, in which these compounds serve as amplifiers of nociceptive input and transmission in both the peripheral and central nervous systems (Malmberg and Yaksh, 1992). The COX-2 selective NSAIDs have been shown to be clinically useful in managing inflammatory pain in humans and animals. This has been a focus of the pharmaceutical industry, as a selective COX-2 inhibitor may potentially show efficacy in alleviating pain and hyperalgesia while sparing COX-1 constitutive activity and potential adverse effects associated with NSAID administration. Unfortunately, the biological system is not as simple as first envisioned. Although COX-2 is induced during inflammation, it also has been shown to be induced during resolution of the inflammatory response in which the antiinflammatory PGs (PGD₂ and PGF₂ α), but not

proinflammatory PGE₂, are produced. Potentially, inhibition of COX-2 during this phase actually may prolong inflammation (Bertolini et al., 2001). As is the case for COX-1, it now appears that the COX-2 isoenzyme also has important constitutive functions. Studies indicate there may be a protective role for COX-2 in maintenance of gastrointestinal integrity, ulcer healing, and in experimental colitis in rats (Reuter et al., 1996; DuBois et al., 1998; Schmassmann et al., 1998). In addition, the COX-2 isoenzyme appears to have constitutive functions associated with nerve, brain, ovarian, and uterine function, and bone metabolism (DuBois et al., 1998). Therefore, the potential for NSAID-associated side effects with these systems is of concern. Of major importance are the COX-2 constitutive functions within the kidney, which differ from those of COX-1 in hypotensive and hypovolemic states (Imig, 2000). Also, COX-2 appears to be important in nephron maturation (Harris, 2000). The canine kidney is not fully mature until 3 weeks after birth, and administration of a NSAID during this time, or to the bitch prior to birth, may cause permanent nephropathy (Horster, Kemler, and Valtin, 1971). In fact, in COX-2 null mice that lack the gene for COX-2, all animals die before 8 weeks of age from renal failure (Morham et al., 1995). This does not occur in COX-1 null mice and interestingly, these mice did not develop gastric pathology (Morham et al., 1995).

When considering the COX selectivity of a particular NSAID, the concentration (i.e., dose) of the NSAID also may influence its actions. A drug may function as a competitive, non-preferential or selective COX inhibitor (COX-1 or COX-2) at higher concentrations, and as a COX-2 selective inhibitor at lower concentrations (Lipsky et al., 2000). The significance of this is the potential for inhibition of COX-1 with administration of an allegedly COX-2 selective NSAID. The COX selectivity may be present in vitro, however, at the dosing required to achieve analgesia, such selectivity may be lost. Cloning studies comparing canine COX isoenzymes with human COX isoenzymes found that they are highly homologous (Gierse et al., 2002). Canine COX-1 and COX-2 had a 96% and 93% DNA sequence homology, respectively, with their human counterparts. This suggests that they would be similarly affected by pharmaceuticals such as NSAIDs designed to inhibit their function. However, the distribution of the COX enzymes may differ among species. When summarizing the common adverse effects noted in veterinary patients following administration of NSAIDs (i.e., gastrointestinal ulceration, renal perturbations, and hemorrhage), hemorrhage is the only one that appears to be spared with COX-2 selective NSAIDs in animals with normal platelet numbers and function.

COX-2 is reduced following administration of glucocorticoids, which may partially explain the antiinflammatory and analgesic effects of this class of medications. Of interest, in addition to the COX-2 role in inflammation, aberrantly upregulated COX-2 expression is increasingly implicated in the pathogenesis of a number of epithelial cell carcinomas, including colon, esophagus, breast, and skin, and in Alzheimer's disease and other neurological conditions (Smalley and DuBois, 1997; Lipsky, 1999; Fosslien, 2000). The COX-2 inhibitors are being researched as potential anti-carcinogenic agents (Fitzgerald and Patrono, 2001).

Dissecting out the details of the derivation and specific actions of COX-1 and COX-2 continues to provide important insight into the management of pain with NSAIDs. However, the picture remains incomplete as some NSAIDS do not significantly inhibit these enzymes. This finding stimulated the search for a potential COX-3 isoenzyme. Based on studies using canine cortex, a COX-3 isoenzyme was discovered that was derived from the same gene as COX-1 (Chandrasekharan et al., 2002). The COX-3 isoenzyme is also present in human brain and heart tissues. It is distinct from COX-1 and COX-2, as demonstrated in studies using common analgesic/antipyretic NSAIDs in suppressing COX production. Acetaminophen inhibited COX-3 activity but not COX-1 and COX-2, as did dipyrone (Chandrasekharan et al., 2002). Both of these agents are frequently used to reduce fever in animals. Other analgesic/antipyretic NSAIDs found to be effective COX-3 inhibitors are diclofenac (the most potent), and aspirin and ibuprofen (which preferentially inhibit COX-3 over COX-1 and COX-2). The overall conclusion of this particular study was that COX-3 possesses COX activity that differs pharmacologically from both COX-1 and COX-2, but is more similar to COX-1 (Chandrasekharan et al., 2002). This study also reported that the COX-3 isoenzyme is more susceptible to inhibition by drugs that are analgesic and antipyretic but that lack antiinflammatory activity. This observation again emphasizes the potential utility of administering NSAIDs with different COX selectivities for managing pain of different etiologies. As the COX-3 isoenzyme genetic profile is derived from the COX-1 gene, it appears that the COX-1 gene plays an integral role in pain and/or fever depending on the physiological context (Chandrasekharan et al., 2002). This has been confirmed by the studies mentioned in the preceding (Ballou et al., 2000; Ochi et al., 2000; Botting, 2003). The COX-1 selective NSAIDs used in veterinary and human patients with poor CNS penetration (i.e., ketoprofen, ketorolac) may, in fact reach sufficient concentrations in the brain to inhibit COX-3 (Warner et al., 1999). It is also recognized that the analgesic effects of these NSAIDs frequently occur at lower dosages than those required to inhibit inflammation.

The NSAIDs and Fever

Just as the relationship between pain and the various activities of the COX system is complex, so too is the association between fever and the COX isoenzymes. The

mechanisms leading to the generation of fever vary depending on the inciting factor, which may be peripheral (i.e., endotoxin) or central (i.e., endogenous pyrogens, such as IL-1). Interspecies variation is also substantial and the definitive role of the COXs in pyesis remains to be clearly elucidated. Evidence suggests that COX-2 plays a role in endotoxin pyrexia, whereas, based on the anti-pyretic effects of acetaminophen and aspirin, COX-1 and COX-3 appear to function in endogenous pyrexia (Botting, 2000; Chandrasekharan et al., 2002; Botting, 2003).

The NSAIDs and Endogenous Antiinflammatory Mechanisms

Endogenously generated small chemical mediators, or autocoids, play a key role in controlling inflammation by inhibiting polymorphonuclear cell recruitment and enhancing monocyte activity in a nonphlogistic manner (Rainsford, 1992). Arachidonic acid–derived lipoxins (LX), particularly LXA4, have been identified as antiinflammatory mediators, indicating that the LOX pathway has a dual proinflammatory and antiinflammatory function.

The NSAIDs may amplify or decrease this endogenous antiinflammatory system. Aspirin is more COX-1 selective and can impair many components of mucosal defense and enhance leukocyte adherence within the gastric and mesenteric microcirculation (Wallace and Fiorucci, 2003). However, with chronic use of aspirin there is an adaptation of the gastric mucosa that is associated with a marked upregulation of COX-2 expression and lipoxin production. This lipoxin is specifically termed aspirin-triggered lipoxin (ATL). Aspirin is unique among current therapies because it acetylates COX-2, thereby enabling the biosynthesis of 15(R)hydroxyeicosatetraenoic acid (15(R)-HETE) from arachidonic acid, which is subsequently converted to ATL by 5-LOX. Inhibition of either the COX-2 or 5-LOX enzymes results in blockade of ATL synthesis (Wallace and Fiorucci, 2003). Lipoxin A4 and ATL (a carbon-15 epimer of LX) attenuate aspirin-induced leukocyte adherence, whereas administration of selective COX-2 inhibitors blocks ATL synthesis and has been shown to augment aspirin-induced damage and leukocyte adherence to the endothelium of mesenteric venules in rats (Wallace and Fiorucci, 2003).

In addition to the lipoxins, aspirin-induced COX-2 acetylation results in the generation of numerous other endogenous autocoids derived from dietary omega-3 fatty acids (Serhan et al., 2002). Some of these local autocoids are potent inhibitors of neutrophil recruitment, thereby limiting the role of these cells during the resolution phase of inflammation, and thus are referred to as *resolvins* (Serhan et al., 2002). The identification of both the lipoxins and the resolvins has introduced new potential therapeutic avenues for the treatment of inflammation, cardiovascular disease, and cancer.

Other Pharmacological Considerations for NSAID Use

Because of their high protein binding NSAIDs can displace other drugs from their plasma protein binding sites and potentially increase their plasma concentration. This is rarely a concern unless administered to animals with organ dysfunction or in those receiving other highly protein bound medications with a narrow therapeutic index. Interference with the metabolism and excretion of certain co-administered drugs may occur; therefore, verifying that the safety of combination therapy is always mandatory.

Some NSAIDs may induce the syndrome of inappropriate secretion of antidiuretic hormone (ADH). Renal water reabsorption depends on the action of ADH mediated by cAMP. As PGs exert a controlled negative feedback action on cAMP production, inhibition of PG synthesis results in above-normal levels of cAMP with potential for enhanced ADH activity. In addition, the administration of a COX-2 selective NSAID may enhance sodium and water reabsorption. Clinically, both mechanisms may result in high specific gravity urine with dilutional hyponatremia. Urine volume may be decreased through this mechanism but without renal injury (Dunn and Buckley, 1986; Petersson et al., 1987).

Contraindications for NSAIDs

Non-steroidal antiinflammatory analgesics should not be administered to animals with acute renal insufficiency, hepatic insufficiency, dehydration, hypotension, conditions associated with low effective circulating volume (i.e., congestive heart failure, ascites), coagulopathies (i.e., factor deficiencies, thrombocytopenia, von Willebrand's disease), or evidence of gastric ulceration (i.e., vomiting with or without the presence of coffee ground material, melena). Administration of NSAIDs following gastrointestinal surgery must be determined by the health of this organ at the time of surgery. As the COX-2 isoenzyme is important for healing, intuitively NSAIDs are contraindicated where compromised bowel is noted. Concurrent use of other NSAIDs (i.e., aspirin) or corticosteroids is not recommended. The COX-1 preferential NSAIDs are contraindicated in animals with spinal injury (including herniated intervertebral disc) because of the potential for hemorrhage and neurological deterioration, and because of excessive bleeding at the surgical site should surgical treatment be pursued. The NSAIDs never should be administered to animals in shock, trauma cases at the time of presentation, or animals with evidence of hemorrhage (i.e., epistaxis, hemangiosarcoma, head trauma). Animals with severe or poorly controlled asthma, or other types of moderate to severe pulmonary disease, may deteriorate with NSAID administration. Aspirin has been documented to exacerbate asthma in human patients; however, COX-2 specific NSAIDs did not result in worsening of clinical signs (West and Fernandez, 2003). It is not known whether animals may be affected in this way. Although administration of NSAIDs in head trauma, pulmonary diseases, or thrombocytopenia is generally contraindicated, COX-2 preferential NSAIDs (i.e., meloxicam, etodolac, carprofen, tolfenamic acid, and deracoxib) may prove to be safe with further study. Because of inhibition of PG activity, the NSAIDs may be detrimental to reproductive function. Indomethacin may block prostaglandin activity in pregnant women, resulting in cessation of labor, premature closure of the ductus arteriosus in the fetus, and disruption of fetal circulation (DuBois et al., 1998). These effects may occur in animals; therefore, NSAIDs should not be administered during pregnancy, as COX-2 induction is necessary for ovulation and subsequent implantation of the embryo (DuBois et al., 1998). NSAIDs also should be avoided in breeding females during this stage of the reproductive cycle. As mentioned, the COX-2 isoenzyme is required for maturation of the embryological kidney, so administration to lactating mothers should be avoided.

NSAIDs Used in Veterinary Medicine

There are little data regarding clinical pharmacology of NSAIDs in exotic species; thus, care must be taken when extrapolating from common domestic species.

Meloxicam (Oral Liquid and Parenteral Formulation)

Meloxicam is a COX-2 preferential NSAID approved for use in dogs in Australasia, Europe, and North America. The parenteral formulation is approved for cats in the United States and Australasia. Its use in cats in Canada is under investigation, with completed studies indicating safety and efficacy. Its use in horses is also under investigation, with pharmacokinetic studies indicating that the half-life is shorter and clearance greater than in the dog, suggesting that dosing more than once a day may be necessary (Sinclair et al., 2003).

Studies indicate no renal or hepatic abnormalities with acute administration and minimal to no antithromboxane activity, suggesting hemostasis in normal animals may not be a problem (Mathews, Pettifer, and Foster, 1999; Poulsen Nautrep and Justus, 1999). Few adverse reactions have been documented and most involve the gastrointestinal tract. A recent study showed no difference in gastric erosions over saline placebo when meloxicam was administered at 0.1 mg/kg for 3 days post-electrical stimulation (i.e., surgical simulation) under anesthesia. However, corticosteroids plus meloxicam in this study resulted in significant gastric erosions (Boston et al., 2003). A case report of combination aspirin and meloxicam in a dog resulted in duodenal perforation (Reed, 2002). This case illustrates the importance of COX-2 in intestinal protection when aspirin is co-administered, and reinforces that different NSAIDs should not be administered concurrently. Analgesia is excellent when meloxicam is combined with an opioid.

Carprofen (Tablet and Parenteral Formulation) Although classified as an NSAID, carprofen administration to beagle dogs did not inhibit PGE₂, 12-hydroxyeicosatetrenoic acid, or thromboxane B2 synthesis in an experimental study using subcutaneous tissue cage fluids (McKellar, Delatour, and Lees, 1994). It was concluded that the principal mode of action of carprofen must be by mechanisms other than cyclooxygenase or 12-lipoxygenase inhibition. However, more recent studies indicate that it is a COX-2 preferential NSAID (Ricketts, Lundy, and Seibel, 1998; Kay-Mugford et al., 2000). Carprofen is approved for perioperative and chronic pain management in dogs in Australasia, Europe, and North America. Carprofen is approved for single-dose, perioperative use in cats in Europe, and is licensed for use in horses in the United Kingdom. In sheep, carprofen (0.7 mg/kg, IV) resulted in plasma concentrations of 1.5 µg/ml, similar to those required to confer analgesia in horses, for up to 48 hours (Welsh, Baxter, and Nolan, 1992). However, analgesia was not assessed in this sheep study (Welsh, Baxter, and Nolan, 1992). Anti-thromboxane activity is minimal, suggesting that induced coagulopathy may not be a problem in animals with intact hemostatic mechanisms (McKellar, Pearson, and Bogan, 1990; Poulsen Nautrep and Justus, 1999).

Ketoprofen (Tablet and Parenteral Formulations) Ketoprofen is approved for postoperative and chronic pain in both dogs and cats in Europe and Canada. Ketoprofen is also approved for use in horses and ruminants. As ketoprofen is an inhibitor of both COX-1 and COX-2, adverse effects are a potential problem requiring careful patient selection. Although several studies using ketoprofen preoperatively indicate its effectiveness in controlling postoperative pain, a general consensus among veterinarians has restricted its use primarily to the postoperative period to reduce the potential for hemorrhage (Pibarot et al., 1997; Mathews, Pettifer, and Foster, 1999; Lobetti and Joubert, 2000). Ketoprofen should not be administered to patients with risk factors for hemorrhage. It is often administered to animals immediately after orthopedic procedures (i.e., fracture repair, cruciate repair, and onychectomy).

Etodolac (Tablet Formulation) Etodolac is COX-2 preferential and is approved in the United States for use in dogs for the management of pain and inflammation associated with osteoarthritis, but is also useful in other painful conditions (Glaser et al., 1995; Budsberg et al., 1999). The adverse effects appear to be restricted to the gastrointestinal tract.

Deracoxib (Tablet Formulation) Deracoxib is a COX-2 specific inhibitor. Deracoxib is approved in the United States and Canada for control of postoperative pain and inflammation associated with orthopedic surgery in

dogs. The incidence of vomiting and diarrhea were similar in dogs receiving deracoxib compared with dogs receiving placebo in a perioperative field trial, and overall the drug was well tolerated and effective (Novartis Animal Health, 2004). It was also shown to be effective in attenuating lameness in dogs with urate crystal-induced synovitis after prophylactic and therapeutic administration (Millis et al., 2002; McCann et al., 2004). This group of NSAIDs appeared to be gastroprotective in human patients when compared with the less COX-2 specific NSAIDs, when used for 8 days to 3 months (Silverstein et al., 2000). However, more recent studies in humans indicate these NSAIDs cannot guarantee gastroprotection with chronic use. Furthermore, in a recent canine study comparing the gastrointestinal safety profile of licofelone (a dual inhibitor) to rofecoxib (another specific COX-2 inhibitor), rofecoxib, was found to induce significant gastric and gastroduodenal lesions (Moreau et al., 2005).

Tepoxalin (Dissolvable Wafer) Tepoxalin is a COX-1, COX-2, and LOX inhibitor of varying degrees with efficacy comparable to meloxicam or carprofen and safety comparable to placebo (Zubrin, 2005). Tepoxalin recently has been approved for management of osteoarthritic pain in dogs. The safety profile of tepoxalin showed no difference from placebo when administered prior to a 30-minute anesthesia period and a minor surgical procedure in dogs (Kay-Mugford et al., 2004).

Tolfenamic Acid (Tablet and Parenteral Formulation)

Tolfenamic acid is approved for use in cats and dogs in Europe and Canada for controlling acute postoperative and chronic pain. The dosing schedule is 3 days on and 4 days off, which must be strictly adhered to. Reported adverse effects are diarrhea and occasional vomiting. Tolfenamic acid has significant antiinflammatory and anti-thromboxane activity; therefore, post-traumatic and surgical hemostasis may be compromised during active bleeding after administration of this NSAID (McKellar, Lees, and Gettinby, 1994).

Flunixin meglumine (Parenteral Formulation) Flunixin meglumine is a COX-1 and COX-2 inhibitor and is approved for use in dogs in Europe but not North America. It is also approved for use in ruminants and horses and is commonly used for equine colic pain.

Phenylbutazone (Powder and Parenteral Formulations)

Phenylbutazone is approved for use in horses, cattle, and dogs in North America. Because safer NSAIDs are approved for dogs, phenylbutazone is not recommended for this species. In horses, there is high risk of gastric ulceration and nephrotoxicity, where signs of toxicity may progress from inappetence and depression to colic, gastrointestinal ulceration, and weight loss

(Snow et al., 1981; Collins and Tyler, 1984; MacAllister et al., 1993). Phenylbutazone has a prolonged elimination half-life in cattle, ranging from 30 to 82 hours (DeBacker, Braeckman, and Belpaire, 1980; Arifah and Lees, 2002).

NSAIDs Not Approved for Use in Veterinary Medicine (Off-Label Use)

Ketorolac (Parenteral Formulation) Ketorolac is a COX-1 and COX-2 inhibitor and is included for the benefit of those working in the research setting associated with human hospitals in which the availability of ketorolac is more likely than other NSAIDs. Adverse gastrointestinal effects are common.

Acetaminophen (Tablet and Oral Suspension Formulations) Acetaminophen is a COX-3 inhibitor with minimal COX-1 and COX-2 effects. It should not be administered to feline species because of deficient glucuronidation of acetaminophen in these species (Court and Greenblatt, 1997).

Aspirin (Tablet Formulation) Aspirin is primarily a COX-1 inhibitor. It has been most commonly used as an analgesic for osteoarthritic pain in dogs. It is also available in proprietary combinations with various opioids (aspirin plus codeine or aspirin plus oxycodone) to achieve a synergistic effect for the treatment of moderate pain. It is also used as an antipyretic and anticoagulant in dogs and cats. Aspirin has also been recommended in cattle.

Dipyrone (Tablet and Parenteral Formulations) Dipyrone is a COX-3 inhibitor and is approved for use in cats and dogs in Europe and Canada. Dipyrone should be given intravenously to avoid the irritation experienced when given intramuscularly. The analgesia produced is not usually adequate for moderate to severe postoperative pain, and dipyrone is reserved for use as an antipyretic in cases in which other NSAIDs are contraindicated. Dipyrone induces blood dyscrasias in humans; however, this has not been reported in animals.

α -2 ADRENERGIC RECEPTOR AGONISTS AND ANTAGONISTS

Introduction

The use of α -2 adrenergic agonists in veterinary medicine began following the synthesis of xylazine in 1962. Early reports of the sedative and anesthetic sparing qualities of xylazine predated the elucidation of its mechanism of action in 1981. α -2 Adrenoreceptors have been identified in the CNS, cardiovascular, respiratory, renal, endocrine, gastrointestinal, and hematologic systems, resulting in widespread drug effects (Aantaa, Marjamaki, and Scheinin, 1995). Most FDA-CVM-approved α -2 agonists carry label indications as sedatives and analgesics.

α-2 Adrenoceptors are linked to Gi-protein second messengers (Aantaa, Marjamaki, and Scheinin, 1995). These are similar to those used by many opioid receptor subtypes and in fact, opioid and α -2 agonists usually have additive or synergistic effects (Maze and Tranquilli, 1991). α-2 Adrenoreceptors are classically described as being located presynaptically at noradrenergic neurons exerting an inhibitory feedback role on the release of subsequent norepinephrine (NE) (Maze and Tranquilli, 1991). This results in decreased sympathetic nervous system efferent activity and probably is related to the decreased vigilance, decreased anesthetic requirements, and decreased heart rate and blood pressure observed following administration of these drugs to most species. α -2 Adrenoreceptors also are found in the vascular smooth muscle (a non-presynaptic site) and when activated result in vasoconstriction. This results in increased vascular resistance and increased baroreceptor-mediated vagal tone. The result is slowing of heart rate and decreasing cardiac output, but blood pressure remains within physiological normal values. Confusion often exists about the clinical effect of α-2 agonist administration (e.g., hypertension (post-synaptic) vs. hypotension (pre-synaptic)) expected in a patient. The net clinical result varies with route of administration, dose, species, and the duration of time following the administration.

 $\alpha\text{-}2$ Agonist doses vary at least 10-fold across species. Pigs tend to have the highest requirements, followed by cats, dogs, horses, and finally ruminants. Breed and sex differences also exist within cattle that should be appreciated.

α-2 Adrenergic Agonist Effects

Central Nervous System α -2 Adrenergic agonists exert many of their inhibitory effects on CNS function through inhibiting NE release from sympathetic neurons (Maze and Tranquilli, 1991). Inhibition of intraneuronal transmission is also responsible for muscle relaxation observed following α -2 adrenergic agonist administration. Analgesia is mediated by spinal and supraspinal α-2 adrenergic receptors. Agonist binding modulates afferent activity at a spinal level and increases the diffuse noxious inhibitory control system activity. The net result is sedation, reduced anesthetic requirements, reduced stress responses, and analgesia. It should be noted that α -2 agonists, like all sedatives and tranquilizers, are not anesthetics. Although animals can appear in a sleep-like state, they may become aroused by noxious stimulation and may become defensive. Additionally, on rare occasions, paradoxical behavior (aggression rather than sedation) may be noted. Accidental intracarotid injection of α-2 adrenergic agonists induces seizure-like activity and must be avoided.

Emetic Center α -2 Agonists are predictable emetics in cats and dogs, especially at high doses. This is caused by

activation of the chemoreceptor trigger zone of the area postrema (Hikasa et al., 1992). Dopaminergic blocking agents do not prevent α -2 induced emesis.

Thermoregulation α -2 Agonists often cause changes in thermoregulation. The effect is usually a decrease; however, increases can be seen when animals are placed in warm environments. This is especially a concern when α -2 agonists are used for capture of cattle or other hoofstock. If possible, body temperature should be monitored for 12 to 24 hours following sedation or administration of an α -2 adrenergic antagonist should be considered. In smaller animals, hypothermia is more common and may result from decreased metabolic activity accompanying sedation as well as decreased thermoregulatory control. It is usually not a life-threatening problem if managed appropriately.

Eye α -2 Agonists generally cause mild miosis to little change in pupil diameter and a mild decrease in intraocular pressure (IOP) (Verbruggen et al., 2000). The class of drugs is relatively contraindicated with increases in IOP or corneal lacerations because of the probability of inducing vomiting (which causes further increases in IOP) in those species that can vomit.

Respiratory System Most α-2 adrenergic receptor agonists can cause decreased responsiveness to CO₂, especially in higher doses. This effect is compounded by the co-administration of opioids or anesthetic agents and is of concern during anesthesia. In some species α -2 agonists do not normally depress respiration to the point of creating hypoxia and cyanosis. In fact, arterial blood gas values for PaO2 are usually normal. The bluish color of the mucous membranes that may be noticed on occasion is usually a result of slowed venous blood flow accompanying vasoconstriction. As the capillary transit time increases, oxygen extraction increases, and notable hemoglobin desaturation appears as a blue(ish) color. Oxygen therapy often resolves this condition. However, in sheep and possibly some other species, xylazine administration has been shown to result in central hypoxemia related to pulmonary changes (Celly et al., 1997, 1999).

Cardiovascular System IV administration of α -2 adrenergic agonists typically results in rapid and pronounced vasoconstriction (Pypendop and Verstegen, 1998). If heart rate and cardiac output do not decrease (as can be seen with atropine administration), blood pressure increases impressively (Short, 1991; Alibhai et al., 1996). However, normal baroreceptor reflexes attempt to maintain blood pressure within physiological limits by increasing vagal tone and slowing heart rate. Heart rate may decrease by 50% to 75% in some individuals. The cardiac rhythm is often a slow sinus rhythm characterized by two or three sequential

beats followed by a long sinus pause. Occasionally, second-degree atrioventricular blockade is seen. Both rhythms are often responsive to antimuscarinic administration (block the vagal reflex), and high heart rates (and blood pressures) result. IM and oral administration tend to decrease the incidence of profound bradycardia.

After the initial direct vasoconstriction occurs, vasodilation and reduction in blood pressure may be seen. This is more prominent in primate species. The $\alpha\text{-}2$ adrenergic receptor agonists decrease sympathetic nervous system efferent activity, which results in decreased vasomotor tone and heart rate. $\alpha\text{-}2$ Adrenergic agonists have been used historically in humans as antihypertensive agents because they reduce vasomotor tone and block the reflex increase in heart rate that can accompany $\alpha\text{-}1$ antagonists.

Most of the contraindications to α -2 adrenergic receptor agonist administration are related to their cardiovascular side effects. As a general rule, this class of drugs should not be administered to animals that do not have normal healthy cardiovascular systems and that are exercise intolerant. There are some exceptions, but a thorough understanding of the underlying disease is required and appropriate monitoring is necessary.

Urinary Tract α -2 Adrenergic receptor agonists increase urine output by increasing production of dilute urine (Grimm et al., 2001; Saleh et al., 2005). This is primarily related to inhibition of ADH release and/or synthesis as well as changes in renal hemodynamics (Saleh et al., 2005).

Gastrointestinal Tract Animals may have complications associated with decreased propulsive activity, including colic and bloat, although this is unusual in most species (Thompson, Kersting, and Hsu, 1991). Longer-acting drugs are more likely to result in a problem. Patients should be observed following α -2 adrenergic receptor agonist administration for signs of abdominal distention.

Endocrine A classic neuroendocrine response is hyperglycemia following α -2 agonist administration (Abdel el Motal and Sharp, 1985; Osman and Nicholson, 1991). This is because of a decrease in insulin release. It is usually transient and not clinically significant, although α -2 agonists should not be used to sedate animals for glucose curves.

Because α -2 agonists reduce sympathetic activity and inhibit the stress response, neuroendocrine markers of the stress response should be affected. Cortisol levels are usually decreased following α -2 agonist administration and may not be reliable as indicators of stress or pain (Brearley, Dobson, and Jones, 1990; Sanhouri, Jones, and Dobson, 1992).

Specific Drugs

Several α -2 adrenergic receptor agonists are approved for veterinary use. Generally, their pharmacological actions are similar, but the duration of action and species compatibility vary. All α -2 agonists are potent and potentially dangerous following accidental human ingestion or injection. Care should be taken when handling syringes loaded with these drugs and medical help should be sought immediately if exposure occurs.

Xylazine Xylazine is the prototypical veterinary α -2 adrenergic receptor agonist. Another α -2 agonist, clonidine, has been used in humans as an antihypertensive agent and is often used as the prototypical drug in research applications. Xylazine has been administered to many different species, both domestic and exotic. It is readily available and relatively inexpensive.

Xylazine has a shorter duration of action than many of the other drugs. Typical doses result in muscle relaxation and sedation of horses for 45 to 60 minutes. This can be advantageous when performing field anesthesia/sedation when a rapid recovery is desired. Xylazine is often combined with opioids such as butorphanol to enhance sedative and analgesic qualities.

Detomidine Detomidine is a longer-acting α -2 agonist approved for use in horses as a sedative. It is commonly administered when profound, long-lasting sedation is needed. When used in high doses as a pre-anesthetic, low respiratory rates may accompany induction. Detomidine is not used in small animals and has not been widely evaluated in exotic species.

Medetomidine Medetomidine is approved for use as a sedative/analgesic in dogs. The drug also has been extensively evaluated in all domestic species and many exotic and zoological species. It is extremely selective for the α -2 receptor and binds avidly. Atipamezole was developed as the specific antagonist for medetomidine for this reason.

Romifidine Romifidine is an α -2 adrenergic receptor agonist that is approved for use in horses. It has been evaluated in other species and appears to be relatively safe, but offers few advantages over other approved products. Some equine clinicians believe is it is a good sedative without causing excessive ataxia.

α-2 Adrenergic Receptor Antagonists

One big advantage α -2 adrenoreceptor agonists have over other sedative/tranquilizers such as acepromazine is reversibility. It is possible to administer an antagonist and within minutes animals regain function and are able to be released. Antagonist administration usually results in opposite hemodynamic effects (e.g., acute vasodilation and tachycardia) and they should not be administered cavalierly. Many of the difficulties

(including some deaths) occur with reversal. Also, α -2 agonist–mediated analgesia is reversed, necessitating administration of other analgesic classes to painful animals. Some species (e.g., domestic horses) are not routinely reversed because of the potential for uncontrollable activity and possible self-trauma.

Yohimbine Yohimbine is a plant-derived compound that has been used by humans for centuries because of its performance-enhancing properties. It is relatively effective for reversing xylazine in horses, dogs, and cats, but is less effective in ruminants. Additionally, yohimbine has some stimulant actions that may result in excitation upon recovery. Yohimbine has not been effective at reversing newer agents such as medetomidine.

Tolazoline Tolazoline was used originally as a therapy for human infants suffering from pulmonary hypertension. It is a relatively non-selective α -receptor blocker and is useful for reducing pulmonary vascular resistance. It is also effective at antagonizing xylazine sedation. It is most commonly used for equine and ruminant species. It appears more effective in ruminant species than yohimbine.

Atipamezole Atipamezole is the marketed antagonist for medetomidine. It is effective at reversing all available α -2 adrenoreceptor agonists and its use is limited only by cost. It is relatively selective for α -2 adrenergic receptors and usually does not cause excessive stimulation, although excitation may occur. Atipamezole is approved for use in dogs; however, it is used in other species commonly. Under most circumstances, it is best given by the IM route except in emergency situations.

NEUROLEPTICS

This class of drugs is typically used as anti-psychotic medication in humans. However, since the 1980s they have been used as effective tranquilizers in wildlife species. The two classes of these drugs used in wildlife are the phenothiazines and butyrophenones. Both of these classes of neuroleptics block the D2-dopamine receptors in the CNS. They reduce dopamine neurotransmission and also have some effect on other dopaminergic, serotonergic, and α -adrenergic receptors. Phenothiazine and butyrophenone neuroleptics are metabolized by hepatic oxidation mechanisms.

Neuroleptics have been very useful in wild ungulate species during capture and relocation programs. These drugs reduce the psychological stress of confinement, isolation, and transport. They can be effective at reducing intraspecies aggression during confinement, as well. Extrapyramidal effects are possible with these drugs, including appetite suppression, Parkinsonism, dystonia, and akathisia.

Neuroleptics often are classified based on their duration of action. The length of action of these drugs has been increased by the development of fatty acid ester formulations of the drug. These drugs are then slowly released over time from depot (injection) sites.

Short-acting neuroleptic drugs include the buty-rophenone tranquilizers azaperone and haloperidol lactate. Both of these drugs are effective tranquilizers and can be given IV or IM. Haloperidol is the only neuroleptic currently available in the United States. Doses used in hoofstock species range from 0.1 to 0.3 mg/kg. Haloperidol lactate typically lasts 12 hours, but has lasted as long as 72 hours in some species. Oral administration at 1 mg/kg may be effective also. Haloperidol is a very effective tranquilizer in antelope and gazelle species.

Most of the long-acting neuroleptics are in the class of phenothiazine tranquilizers. All of the long-acting neuroleptics should only be given IM. Zuclopenthixol acetate has an onset of action of a few hours and may last for 4 days. Perphenazine enanthate typically has a 12- to 16-hour onset of action and lasts up to 10 days. Pipotiazine palmitate may have a 72-hour onset of action and may have an effective duration of up to 21 days.

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EuthanasiaMurray Woodbury

INTRODUCTION

Euthanasia is the act of humanely causing the death of an animal. To be considered euthanasia rather than just the termination of a life, the act must minimize any pain, distress, or anxiety experienced by the animal prior to its death. An ideal euthanasia technique would induce a very rapid loss of consciousness in the animal, followed by cardiac and respiratory arrest and the loss of brain function (AVMA, 2001). The method would also be reliable, irreversible, and relatively safe for the operator. This ideal method and indeed many of the recommended techniques for domestic and laboratory animals are usually not possible in the zoo or under field conditions, in which many of the factors involved with euthanasia are not well controlled. Under these circumstances the taking of an animal's life is more often humane killing rather than euthanasia. In zoos and wildlife environments, consideration for factors such as degree of control over the animal, operator and public safety, species peculiarities, and carcass disposal may result in some unavoidable pain and anxiety associated with a rapid and efficient death.

Wildlife and zoo veterinarians and any other persons involved with animal research or management are ultimately responsible for the animals under their influence and should be prepared for the possibility of euthanasia in irreversibly diseased or injured animals. They should be familiar with the available techniques for the species and obtain and prepare the required materials and equipment in advance so that correct euthanasia is possible if necessary. Persons actually performing euthanasia should have the appropriate training and experience to ensure that pain and distress are minimized during the procedure.

CONSIDERATIONS FOR WILDLIFE AND ZOO SPECIES

The primary consideration should be providing a quick and painless death whenever possible. In wildlife and

zoo situations in which the animal is not well confined or restrained, this sometimes means the use of an appropriate-caliber firearm to inflict a fatal wound. In freeranging animals a fatal headshot may be difficult to accomplish and accidental injury to the animal or an unintended target may be the result. A shot to the heart and lungs is more easily achieved and requires less skill from the operator. Death in this case is not as rapid but is much more certain under free-ranging conditions (CCAC, 2003). In other situations whenever possible the chosen method or combination of methods should involve the use of a chemical or physical technique that first depresses the central nervous system (CNS) to ensure immediate insensitivity to pain and relief from distress, fear, and apprehension; followed by the irreversible arrest of the animal's respiratory and cardiac function and brain death.

The practical problems associated with disposal of one large or several individual euthanatized animals and the environmental risks posed to animal scavengers or humans in contact with a carcass euthanatized with toxic chemicals also must be considered. Incineration, burial, or adulteration of the carcass with quick lime is acceptable but not always possible, especially with megavertebrates or marine mammals. A chemical-free euthanasia protocol should be used when carcass disposal is not practical or possible.

Consideration should be given to the collection of postmortem samples for diagnostic or research purposes. When animals are sacrificed for scientific study or disease surveillance, the method of euthanasia should not destroy the tissues or organs of interest. For instance, a gunshot to the brain is not appropriate when animals are to be tested for rabies or other CNS diseases.

METHODS

The choice of a suitable method of euthanasia depends on the species, size, weight, and behavioral characteristics of the animal. The type of restraint possible, the facilities and equipment available, the number and skill of assisting personnel, and the risks involved should be considered. Economics and the number of animals to be euthanatized also can affect the decision.

Literature specific to the species of interest should be consulted when planning euthanasia or activities that could result in euthanasia. Detailed recommendations for euthanasia can be found in the 2000 Report of the AVMA Panel on Euthanasia (AVMA, 2001) and the Guidelines on Euthanasia of Nondomestic Animals (AAZV, 2006). Much of the information in this chapter is derived from these sources.

Depending on the chosen method of euthanasia, death results from hypoxia, CNS depression, physical damage to the brain, or a combination of these mechanisms. The means of inducing these changes can be chemical, physical, or electrical (Table 2.1). Current guidelines on euthanasia (AVMA, 2001) classify methods as recommended, conditionally acceptable, or generally unacceptable. Conditionally accepted methods are those that may be acceptable for emergencies, or unplanned euthanasias, when rapid killing rather than true euthanasia is achieved. Some unacceptable methods may become acceptable when used in euthanasia protocols in which deep anesthesia is provided prior to using the method. Such combined methods are called two-stage protocols and are especially important when animals cannot be adequately restrained to receive primary methods, such as intravenous euthanasia drugs or a precisely applied physical means of euthanasia. The first stage generally renders the animal unconscious so that it can be approached or humanely restrained for a lethal secondary procedure.

The use of immobilizing drugs followed by a chemical or physical method of euthanasia should be considered to gain control over the movements of free-ranging animals or when close restraint is either too stressful or impossible to achieve in a zoo setting. Immobilizing doses of sedative drugs, usually delivered by a dart gun or blow pipe, can be used to induce a rapid loss of consciousness, permitting the operator direct contact with the animal to subsequently administer suitable chemical or physical euthanasia. An important historical exception to this sequence is when succinylcholine is used as the immobilizing drug (Schwartz et al., 1997). Succinylcholine rapidly induces paralysis but offers no analgesia or relief from distress or anxiety and its use as a primary method for euthanasia is not acceptable. In the past it has been used in free-ranging wildlife because of its rapid onset and relatively low risk posed from drug residues in the euthanized animal (AVMA, 2001). However, it is imperative to reach the paralyzed animal as quickly as possible to render it unconscious and insensitive using a secondary method such as a gunshot or penetrating captive bolt to the head. In the case of free-ranging animals, such rapid acquisition of the target animal usually is not possible and a lethal gunshot

should be used as the primary method. In zoo situations alternate drugs for rendering animals insensible are available, making succinylcholine an obsolete and unacceptable drug for use in euthanasia protocols.

ASSESSING DEATH

Verification of death is important for ethical and safety reasons. Animals that recover from attempts at euthanasia can harm nearby personnel through violent physical struggle or defensive acts. Assessing whether death has occurred is especially important when euthanizing potentially dangerous animals and animals that can withstand long periods of anoxia. It is essential that personnel involved with euthanasia be trained to confirm death in the species of concern.

Signs of death include absence of breathing movements, absence of a pulse or heartbeat, discolored mucous membranes with no capillary refill, dilated and fixed pupils, and loss of the corneal reflex. Because none of these signs is universally consistent across species, a physical method of euthanasia such as decapitation or exsanguination should be used as a final step if there is any doubt that death has occurred.

SPECIFIC RECOMMENDATIONS

Birds

The method most often recommended for birds is the parenteral administration of sodium pentobarbital, preferably intravenously. Exposure to carbon dioxide gas is conditionally acceptable and can be used for euthanasia of large numbers of birds. It is also the only chemical method useful for birds intended as food. An overdose of inhalant anesthetics such as halothane, isoflurane, and sevoflurane is also conditionally acceptable but should be followed by a method that precludes recovery. Cervical dislocation, stunning, decapitation, or methods causing destruction of the brain such as gunshot to the head or penetrating captive bolt are all conditionally acceptable. Methods that are generally unacceptable for birds include potassium chloride injection, thoracic compression, exsanguination, and induction of hypothermia or rapid freezing in liquid nitrogen or dry ice. When eggs with less than 50% of incubation time are involved, addling (shaking), puncture, freezing, or coating the shell with oil are suitable means.

Amphibians and Reptiles

Euthanasia of amphibians is facilitated by their ability to absorb anesthetic drugs through their skin, making immersion in solutions of tricaine methanesulfonate (MS-222) or benzocaine HCl the recommended primary method in these species. Secondary methods, such as decapitation, cervical dislocation, or exsanguination, should always follow. Electrical or concussive means of stunning followed by decapitation can be conditionally

Table 2.1. Euthanasia methods fo	Euthanasia methods for wildlife and zoo species.		
Method	Primary Method for these Species	Secondary Method for these Species	Comments
Inhalant agents Volatile anesthetic agents		Amphibians, reptiles, small and medium mammals, hoofstock	Requires a follow-up method to ensure death. Not generally suitable in the field or for species that breath hold or having low respi-
Carbon dioxide		Amphibians, reptiles, small and medium mammals, hoofstock	ratory rates. Concentration of CO_2 must be >40% of inspired air. Can be used to render food animals unconscious but not generally recommended
Carbon monoxide		Reptiles, small and medium mammals, hoofstock	for euthanasia. Concentrations > 10% in air are explosive. Odorless gas is toxic to humans and generally
Nitrogen, argon		Small and medium mammals	not used for safety reasons. Generally safe for operator. Motor activity con tinues until death, which can be disturbing to viewers.
Chemical agents			
Barbiturates	All species		Ideal for most species, but in amphibians and reptiles a secondary physical method is recommended. Creates carcass disposal
T-61	All species		problems from secondary toxicity. A controlled drug needing accounting. Mixture of three drugs. Must be used IV. Not as smooth as barbiturates. Not available in all
Tricaine methane sulfonate (MS 222), benzocaine HCl	Fish, amphibians		countries. Leave animal in water bath for >10 minutes after respiration ceases. Requires buffering and disposal. Follow-up
Potassium chloride		Amphibians, small and medium mammals,	inetitiod needed to ensure deatin. Give by IV or intracardiac injection. Use only on anesthetized animals
Neuromuscular blockers (succinylcholine, gallamine)		Reptiles, medium mammals, hoofstock, and megavertebrates	Unsuitable method for primary euthanasia, but in limited circumstances might be useful for initial immobilization if followed rapidly by
Formalin, alcohols		Amphibians, small reptiles	acceptable method. Prior anesthesia needed. Very small animals only.
			(Partition)

Table 2.1. (Continued)			
Method	Primary Method for these Species	Secondary Method for these Species	Comments
Physical methods			
Gunshot to the head, cervical neck	Unrestrained medium sized mammals, hoofstock, and megavertebrates	Large reptiles, small and medium mammals, hoofstock,	Appropriate for free-ranging animals in secluded areas or as secondary method. Requires operator training and skill. Safety
Stunning (concussion or electric)		Amphibians, reptiles, small mammals	Generally used in emergency situations when no other means available. Should be followed by cocondary method or a systematical and a systematical
Penetrating captive bolt to the head	Restrained hoofstock	Hoof-stock	Adequate restraint or anesthesia needed prior to use. Operator training, skill, and specialized
Cervical dislocation		Small mammals	Small animals only (<200 g). Prior anesthesia recommended.
Pithing		Amphibians, reptiles	Prior anesthesia needed. Generally used as a secondary method.
Decapitation		Amphibians, reptiles, small mammals	Prior anesthesia needed. Generally used as a secondary method.
Thoracic compression Exsanguination		Amphibians, reptiles Amphibians, reptiles, small and medium mammals, and megavertebrates	Not suitable for animals with a diaphragm. Not a primary method of euthanasia. Useful as a secondary method or confirmation of death.
Hypothermia/rapid freezing Kill traps Explosives	CNS destruction, anoxia	Amphibians, small reptiles, small mammals Small and medium mammals Megavertebrates	Prior anesthesia needed. Not acceptable in most applications. Generally not recommended, except when no other means available.

Sources: Guidelines on Euthanasia of Nondomestic Animals, American Association of Zoo Veterinarians (AAZV 2006) and the 2000 Report of the AVMA Panel on Euthanasia (AVMA 2001).

acceptable in circumstances in which other methods are not available. Methods that are unacceptable as the sole means of euthanasia include injection of potassium chloride, pithing, exsanguination, and induction of hypothermia or rapid freezing by immersion in liquid nitrogen or dry ice.

Parenteral injection of sodium pentobarbital is recommended as a stand-alone method for both amphibians and reptile species. Conditional chemical methods include inhalation of carbon dioxide gas or fluorinated gas anesthetics such as halothane. Other conditional means are concussive stunning, decapitation followed by pithing, cervical dislocation, and for species such as crocodilians, captive bolt penetration of the brain. Immersion of smaller reptile species in formalin, formaldehyde, or ethanol is not acceptable without prior deep anesthesia. Potassium chloride injection, carbon monoxide asphyxia, and the use of neuromuscular blockers such as succinylcholine or gallamine without prior general anesthesia is unacceptable. Pithing, exsanguination, hypothermia from ice packing, and rapid freezing with liquid nitrogen or dry ice are unacceptable except when they are used in a two-stage protocol.

Small and Medium-Sized Mammals

The method most often recommended is sodium pentobarbital injection, preferably intravenously, but also via intracardiac and intraperitoneal routes under some circumstances. Inhalation anesthetics such as halothane, isoflurane, and sevoflurane as well as carbon dioxide gas are conditionally acceptable in small mammals provided another method, usually physical, is used to ensure the termination of life. Physical methods such as cervical dislocation or decapitation in smaller species, and gunshot or penetrating captive bolt to the head can be used in medium-sized mammals that are under general anesthesia at the time. Thoracic compression is not suitable in mammals because of the presence of a diaphragm, nor is the induction of hypothermia by refrigerator, refrigerated water, or ice. Rapid freezing with liquid nitrogen is only appropriate for very small mammals already under general anesthesia or newborns and fetuses less than 4 g. Administration of gaseous carbon dioxide, carbon monoxide, argon, or nitrogen is generally unacceptable unless preceded by general anesthesia. Neuromuscular blockade by drugs such as succinylcholine is not appropriate as a sole method of euthanasia, but can be used in some circumstances as chemical restraint in a two-stage procedure when followed rapidly by a suitable means of humane killing so that asphyxia and distress are minimized.

Hoofstock

In addition to the generally recommended sodium pentobarbital injection, which can be expensive in large animals, administration of a penetrating captive bolt to the brain followed by exsanguination is a recommended method for euthanasia of hoofstock. However, both methods require adequate restraint and close contact with the animal to be effective. Remote delivery of drugs inducing general anesthesia followed by performance of the above methods on an immobilized animal is often best.

Succinylcholine has been used in some circumstances as a chemical restraint drug in two-stage procedures followed by rapid killing so that asphyxia and animal distress are minimized. However, succinylcholine is not appropriate as a routine immobilizing agent or the sole method of euthanasia. This drug does not render animals unconscious or provide any physical or emotional pain relief. Its use without adjunct drugs or procedures is inhumane and therefore unacceptable (AVMA, 2001).

Conditionally acceptable methods applied to hoofstock theoretically include lethal administration of gas anesthetic agents such as halothane or isoflurane and gunshot to the head or cervical spine region. The latter method, although useful in situations in which handson methods are not possible, requires operator skill and experience and a suitable firearm and ammunition. Administration of carbon monoxide gas, intravascular or intracardiac potassium chloride solution, or exsanguination is not acceptable without prior general anesthesia.

Megavertebrates and Marine Animals

Injection of sodium pentobarbital, although also ideal in these species, requires adequate restraint and large, costly volumes of drug. Prior administration of general anesthesia-inducing drugs such as potent narcotics can facilitate euthanasia with barbiturate. Penetrating captive bolt guns are generally ineffective in such large animals. Gunshot to the head or cervical region of large terrestrial species such as elephants and rhinoceros can be appropriate as the sole means of humane killing in some emergency situations and at some locations but is much less effective with large species such as whales. Explosives have been used to euthanatize beached whales, but this method is generally not recommended because of the high level of expertise required and the inherent danger to personnel. Exsanguination is usually acceptable only when used secondary to a procedure that first renders the animal insensible.

SUMMARY

The best method of euthanasia for most captive and free-ranging wildlife involves the use of two-stage protocols in which the animal is first rendered insensible and then its life is terminated by some efficient and irreversible means. In those situations in which immediacy and urgency dictate that a more direct method be employed, especially for medium to large species, the use of a firearm is often the quickest and most practical

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way to humanely end an animal's life under the prevailing circumstances.

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Wildlife Analgesia Karen L. Machin

WHAT IS PAIN?

Pain is defined by the International Association for the Study of Pain (IASP) as "an unpleasant sensory and emotional experience associated with actual or potential tissue damage, or described in terms of such damage." The IASP also has noted that inability to communicate in no way negates the possibility that an individual is experiencing pain or is in need of appropriate pain-relieving treatment. If an animal is incapacitated to the point that it cannot respond, it does not mean that it is not experiencing pain or does not require therapy. Overwhelming scientific evidence supports that animals can experience or feel pain. Suffering can be an important component of the pain experience because animals cannot understand that pain may be relieved or subside in the future. This is reflected by the American Veterinary Medical Association's position statement "that animal pain and suffering are clinically important conditions that adversely affect an animal's quality of life" (AVMA, 2001). Procedures or conditions known to cause pain in humans also should be considered to be painful in animals (Morton and Griffiths, 1986). Where possible pain should be treated or prevented.

WHO EXPERIENCES PAIN?

A consensus statement made by participants of the Mayday Fund-sponsored workshop, A Cross-Species Approach to Pain and Analgesia, states:

It is unclear at this time at what taxonomic level nociception is associated with pain and whether all species, including humans, feel pain with the same qualities and intensities. Operationally, vertebrates and some invertebrates experience pain (Paul-Murphy, Hess, and Fialkowski, 2004).

In contrast to the conscious experience of pain, nociception is the unconscious detection of transmissions

and responses to noxious simulation by the nervous system. Nociception is the sensory aspect resembling our pain, without subjective reactions and suffering (Mather, 2001). All animals possess neuroanatomical and neuropharmacological components necessary for transduction, transmission, and perception of noxious stimuli (Flecknell, 1994; Machin, 1999, 2001, 2005; Paul-Murphy, Hess, and Fialkowski, 2004); however, it is unclear if all species have an "emotional response." A general assumption is that capacity to experience pain and distress is directly related to phylogenetic position, that is, Mammalia > Aves > Reptilia > Amphibia > Pisces > Invertebrata (Stevens, 1992). When debating the issue of pain versus nociception, taxonomic differences in complexity of the central nervous system (CNS) anatomy has been used as criterion for the pain experience. Although higher degrees of encephalization imply greater self-awareness, retrospection, anticipation of future events, and potential for mental distress, this may have minimal effect on immediate, acute perception of and response to pain. Rather than trying to ascertain at what phylogenetic level nociception becomes pain in animals, it may be more appropriate to consider the evolutionary value of pain as an essential element for survival (Paul-Murphy, Hess, and Fialkowski, 2004).

Most clinicians assume that vertebrates have a greater capacity to experience pain than invertebrates. This different attitude to vertebrates and invertebrates is also reflected in legislation of animal welfare of most countries (Sømme, 2005). More recently a report suggested that invertebrate species with relatively complex brains are aware of their surroundings and probably feel pain and experience stress. The presence of opioids in a variety of invertebrates suggests that modulation of adverse and nociceptive responses was present at an early stage of evolutionary history (Kavaliers, 1988). Separation of vertebrates and invertebrates early in evolution of the animal kingdom may suggest that fundamental differences in the CNS and sense organs may have evolved (Sømme, 2005). In addition to

morphological differences, brain electrical activity of invertebrates differs from those of vertebrates and some cephalopods (Bullock, 1984). Differences in brain signals between vertebrates and invertebrates may depend on different anatomical arrangements of neurons and their processes (Sømme, 2005). Escape mechanisms in animals are essential adaptations partly based on reflexes, and not necessarily associated with conscious experience. Rapid withdrawal in invertebrates is often based on short neural circuits from neural cells to muscles. To different degrees, behavior is also modified by learning, especially in octopuses and social insects (Sømme, 2005).

In cephalopods, reactions to noxious stimuli produce avoidance and escape reactions. Cephalopods have a CNS, which is often described as a brain. Squid and octopus have a great ability to learn and alter their behavior in response to or to avoid a subsequent noxious stimulus, which suggests they are also likely to experience pain. Although it is not known if cephalopods have emotions, there is evidence of aversion, emotion-like responses, exploration, play, and cognitive ability to negotiate difficult dilemmas that resemble responses of higher vertebrates to threat and pain (Mather, 2001; Sømme, 2005).

WHY TREAT PAIN IN WILDLIFE?

It is almost certain that any free-living creature will experience some discomfort, pain, and/or suffering at some point in its life; so why should we treat for pain? As humans studying these creatures in the wild or caring for them in a captive situation, we have a moral obligation to ensure that animals in our care are treated humanely. Humane treatment requires alleviation of pain, distress, and suffering. Not only is there ethical benefit, but animals suffer deleterious effects if not treated appropriately for pain. Unrelieved pain can result in behavioral changes, weight loss, muscle breakdown, impaired respiratory function, increased blood pressure, and possible extended periods of convalescence. Untreated or unmanaged pain may lead to selfmutilation and potential development of chronic pain states (Robertson, 2001). Without treatment animals may not behave normally, which can alter data collected from experimental studies. Altered behavior may predispose to expulsion from a group or predation. With renewed public emphasis on captive wild animals, circus, and aquarium animals, spectators also may demand high standards of care or complain when they see something they perceive as cruelty.

Recognition of pain and its prevention or treatment can certainly be challenging for anyone working with wildlife, either captive or free-ranging animals; but regardless, pain prevention and treatment should be part of any husbandry or study protocol. Observers should become familiar with normal behavior of different species and care should be taken not to misinterpret

the activity or inactivity as a lack of pain perception. Species that are preyed upon display less overt painassociated behavior in an attempt to avoid attracting the attention of predators (Livingston, 1994). Prey species may remain immobile during examination by "playing dead," but again this should not be misinterpreted as a lack of response to pain (Flecknell, 1994). Diurnal observation of nocturnal species also may yield inaccurate behavioral information. Given the diversity of wildlife species and considerable variation in behavioral responses to different pain states occurring among species as well as individuals, practitioners and researchers must keep in mind that there is no reliable or universal indicator of pain. In many cases this leads to a development of subjective evaluation, but where possible this information should be shared in the form of publications or conference presentations.

Many current treatments for animals are extrapolated across species boundaries and from laboratory to clinical settings, often without verification or validation (Paul-Murphy, Hess, and Fialkowski, 2004). It is clear that for any particular drug, some species respond in a similar manner, whereas others respond quite differently (Halpin, Geer, Zhang, 2000). In mammals, the majority of information about pain has been gained from laboratory, companion, and farm animals, and it is recognized that there is a wide range in response to painful stimuli among mammalian species, breeds, and individuals. In contrast, information about wild mammals and other species is limited and has been derived from only a handful of species. However, our knowledge of animal pain has increased considerably in recent years both in terms of our understanding of physiological and pathological processes associated with different pain states and in our knowledge of mechanisms and actions of analgesic agents (Livingston, 2002). With further research and the sharing of information, analgesia in wildlife species will become a more exact science.

PAIN PHYSIOLOGY

Please note that information given here is based on mammals. For phyla and species specific information, please refer to the phyla sections that follow.

Types of Pain

Pain is a perceptual experience that is commonly associated with tissue-damaging stimuli and can induce distress and suffering. Acute pain is an evolved protective mechanism that allows for prevention of further damage and enabling of healing and tissue repair. Chronic pain has little or no protective value and produces changes in the nervous system that can escalate and alter sensory inputs, resulting in physiological, metabolic, and immunological alterations that threaten homeostasis and contribute to illness and death (Muir, 2001). Physiology of pain involves two

processes: (1) a peripheral process involved with detection and transmission of information concerning potential tissue damage; and (2) a central process governing the cerebral response to this information. A noxious stimulus is defined as a potentially tissue-damaging stimulus and a receptor sensitive to a noxious or potentially noxious stimulus is termed a nociceptor. Noxious stimuli elicit reflex withdrawal as well as behavioral, autonomic nervous system, neuroendocrine, and immune system responses in proportion to the severity of the stimulus (Chapman et al., 1985). Nociception is the detection of a noxious stimulus and transmission of that information to the brain (Muir, 2001).

Pain involves activation, modulation, and modification of primary sensory and central neurons. Nociceptive pain or physiological pain involves a noxious stimulus that induces minimal or no tissue damage. It activates high-threshold sensory nerve fibers, warning the organism of potential tissue damage. This is very important because it initiates a protective reflex, involving physiological and behavioral (avoidance) responses. Physiological pain is well localized and transient (Willis and Westlund, 1997). In comparison, when excessively intense or prolonged stimuli induce tissue damage resulting in extended discomfort and potentially abnormal sensitivity, this is clinical pain. It can be caused by inflammation associated with tissue damage (inflammatory pain) or central or peripheral nerve injury (neuropathic pain) and may be induced by stimuli not normally considered painful (allodynia) (Muir, 2001).

Tissue injury and acute pain can affect both peripheral and central nervous systems and alter sensitivity to subsequent stimuli. This "sensitization" may be characterized by: (1) a response to pain at a lower stimulus level (lower activation threshold); (2) an increased response to noxious stimuli; (3) a response to pain more quickly (shorter response latency); (4) a longer duration of response to stimulation (persistent pain); (5) an increased response to a given stimulus intensity or spontaneous activity; (6) and/or spread of pain and hyperalgesia (increased response to a stimulus that is normally painful) to uninjured tissue (Chapman et al., 1985). Tissue injury can induce prolonged changes in CNS function that later influences responses to subsequent afferent inputs and contributes to postoperative pain (Katz et al., 1992). Peripheral sensitization is a reduction in threshold to painful stimuli on exposure of the nerve terminal to sensitizing agents and is caused by inflammation at the site of tissue damage or trauma. This peripheral sensitization can be augmented by sympathetic nervous system interactions with primary sensory afferent nerves (Woolf and Chong, 1993). Nociceptive information that reaches the spinal cord can produce central sensitization (a state of spinal neuron hyperexcitability). Central sensitization occurs when the threshold required to activate dorsal horn neurons decreases following activity of nociceptors.

Recruitment of other nerves as a result of increased output or increased excitability causes changes in receptive field properties (Chapman et al., 1985). Intense or prolonged noxious stimulation may cause alterations in patterns of gene expression, altering phenotype of neurons and providing the nervous system with a substantial degree of neuroplasticity (Pockett, 1995). It is important to remember that pain-induced neural changes can be prevented by administration of analgesic agents before development of injury induces spinal hyperexcitability and pain-related behaviors (Katz et al., 1992; Woolf and Chong, 1993).

ANALGESIA

Analgesia is the relief of pain without loss of consciousness. Analgesics decrease stimulation of ascending spinal pathways or activate endogenous descending pain modulation pathways (Livingston, 1994). Experimental evidence shows that there is a relationship between activation of nociceptors and behavioral evidence of pain (Gentle, 1992). Recognition of pain and anxiety in animals is critical for appropriate analgesic selection and pain relief. Controlling pain not only involves pharmacological administration, but also should include physical, environmental, and behavioral management (Wright, Marcella, and Woodson, 1985). Proper care and non-pharmacological methods of analgesia include: support or bandaging of the traumatized area; appropriate environmental modification with proper choice and location of perches, bedding, food, and water; and provision of a dry, warm, quiet, nonstressful environment. These should be included in any pain management program. Reduction of fear and anxiety with anxiolytics, tranquilizers, and muscle relaxants also can reduce muscle tension and CNS activity (Clyde and Paul-Murphy, 1999). However, not all of this may be practical in free-ranging wildlife. Reduction of stress during handling periods and returning the animal to its normal environment or a temporary holding pen for recovery may be more important to prevent loss of family units or disruption of pair bonds and allow for return to normal function and behavior.

Appropriate and timely administration of analgesics is important, as persistent pain perception can have a negative effect on homeostasis and healing (Wright, Marcella, and Woodson, 1985). Provision of analgesia prior to injury can lesson or prevent pain from occurring. Tissue injury can induce prolonged changes in CNS function that later influences responses to subsequent input and contributes to postoperative pain. Nociceptive information that reaches the spinal cord can produce central sensitization. Studies in mammals show that pain-induced neural changes can be prevented by administration of analgesic agents before development of injury induces spinal hyperexcitability and pain-related behaviors (Katz et al., 1992). Analgesics

administered after prolonged central excitability or pain behavior has been established may be less effective. Preemptive analgesia blocks sensory stimuli transmission, thus reducing overall pain experienced by the animal (Katz et al., 1992). If at all possible analgesia should be administered to patients prior to surgery. When injury occurs prior to surgical intervention, analgesia should be administered as soon after injury as possible and maintained, and if possible, as long as the animal is displaying pain-related behavior.

Balanced anesthesia refers to administration of several drugs to prevent excess physiological derangements by any single drug during or after anesthesia (Concannon, Dodam, and Hellyer, 1995). A balanced approach to anesthetizing patients can minimize adverse effects of any single drug and agents may maximize analgesia. Administration of appropriate analgesics perioperatively will reduce the amount of inhalant anesthesia required, thus increasing safety during the procedure. Opioid or α_2 -agonists decrease requirements for inhalant anesthetics in a dose-dependent manner, thus decreasing minimum alveolar concentration (MAC). MAC (or in species without alveoli, minimum anesthetic concentration) is the concentration of anesthetic that produces no response in 50% of patients to a painful stimulus. However, care should be taken when combining opioids and α_2 -agonists because of potential for respiratory depression in many species (Concannon, Dodam, and Hellyer, 1995).

Opioids are frequently used for acute pain control, often perioperatively. Not only are opioids highly effective analgesics for moderate to severe pain, but also they may be given preoperatively to provide sedation and aid restraint. Opioids tend to be relatively sparing of the cardiovascular system and their use as a premedication allows for a decrease in amount of other, more cardiovascularly depressant agents needed to provide anesthesia (Pascoe, 2000). Opioids produce analgesia by their actions on specific opioid receptors (mu (μ), kappa (κ), delta (δ)), mimicking effects of endogenous opioids (endorphins, enkephalins, dynorphins). These receptors vary in their distribution throughout the body and pharmacological effects (although all three produce analgesia) (Waldhoer, Bartlett, and Whistler, 2004). Opioids activate pain-modulating neurons that project into the spinal cord and inhibit transmission from primary afferent nociceptors to dorsal horn sensory projection cells. They act by reversible combination with one or more specific receptors in the brain and spinal cord to produce a variety of effects, including analgesia, sedation, euphoria, dysphoria, respiratory depression and excitement, hypotension, hypothermia, urine retention, and emesis.

Pure opioid agonists include morphine, meperidine, oxymorphone, hydromorphone, fentanyl, sufentanil, and carfentanil, and bind to one or more opioid receptors subtypes (Waldhoer, Bartlett, and Whistler, 2004).

They provide profound analgesia to patients with moderate to severe pain (Perkowski and Wetmore, 2006). Butorphanol and buprenorphine have opioid agonist-antagonist potency agonists and are not considered adequate for significant trauma or bone pain. Their use may be preferred in certain situations because of less severe side effects. These drugs have a ceiling on the maximal effect they cause, so despite additional drug administration, no improvement in analgesia can be achieved over that obtained from one maximal recommended dose. Administration of these agents may partially reverse effects of previously administered pure agonists. This may be advantageous if you are trying to reverse sedation or respiratory depression, but it will also reverse some of the analgesia (Perkowski and Wetmore, 2006).

Effects of opioids can be competitively reversed by the antagonist naloxone and partial antagonists nalorphine, butorphanol, and buprenorphine. Naloxone (0.01–0.02 mg/kg IM or IV slowly) will reverse undesired effects, but it is important to provide cardiovascular and respiratory support if needed. Small doses of butorphanol (0.05–0.1 mg/kg) may be titrated to reverse some sedative effect of a pure opioid agonist, while retaining some of the analgesia by enhancing κ effects (Perkowski and Wetmore, 2006). It is very import to keep in mind that completely reversing opioids also results in loss of analgesia (Flecknell, 1988).

 α -Adrenoreceptors are located in several areas within the spinal cord and brainstem concerned with analgesia. When given systemically, α_2 agonists (e.g., xylazine, detomidine, and medetomidine) produce analgesia, anxiolysis, sedation, and reduction in MAC of inhalant anesthetics. Administration of α -adrenoceptor agonists produces dose-dependent analgesia (Brenner et al., 1994; Stevens and Brenner, 1996). They also produce pronounced cardiovascular side effects, including vasoconstriction-associated hypertension, which is followed by hypotension secondary to a decrease in norepinephrine release and sympathetic outflow centrally, with pronounced decreases in heart rate and cardiac output. They may cause respiratory depression, emesis, and increased urine production (Murrell and Hellebrekers, 2005). They are most commonly used for anesthesia but provide analgesia at the same time. Low doses (0.5–3 µg/kg/hour) of intravenous medetomidine have been shown to provide analgesia with minimal cardiovascular effects (Pascoe, 2006). Analgesic effects appear to be mediated by α_2 - receptors since pretreatment with selective α_2 -antagonists, yohimbine, and atipamezole inhibit analgesic effects (Brenner et al., 1994).

Local anesthetics (such as lidocaine and bupivacaine) function by blocking ion channels, thereby preventing generation and conduction of pain impulses (Courtney, 1980). Local anesthesia administered before tissue trauma can reduce postoperative pain significantly because it prevents nociceptor sensitization and avoids central changes that are secondary to activation of pain pathways. Local nerve blockade administered before nerve transection in amputation can decrease prevalence of phantom limb pain in humans. Local anesthetics are extremely useful for providing analgesia for pain arising in discrete locations (Flecknell, 1988; Wright, Marcella, and Woodson, 1985).

Prostaglandins (PGs) are important local mediators of inflammation and pain, and are also known to lower activation threshold (response to pain at a lower stimulus level) to thermal, mechanical, and chemical stimulation. Nonsteroidal antiinflammatory drugs (NSAIDs) control pain by inhibiting cyclooxygenase enzyme (COX), which prevents the production of PGs (e.g., prostaglandin E2), prostacyclin, and thromboxane (Machin, 2005). Many of these metabolites are important mediators of the peripheral inflammatory response that contributes to peripheral hypersensitization. More recently, it has been recognized that NSAIDs produce much of their analgesic effect by inhibiting COX activity centrally (Beiche et al., 1996). These drugs do not cause sedation, excitement, respiratory depression, or hypotension when used at therapeutic doses (Perkowski and Wetmore, 2006).

The COX enzyme exists in at least two isoforms, COX-1 and COX-2 (recently, a COX-3 isoform has been identified in the brain) (Chandrasekharan et al., 2002). Prostaglandin synthesis is mediated by one of two isoforms of cyclooxygenase enzymes: cyclooxygenase-1 (COX-1) and cyclooxygenage-2 (COX-2). The COX-1 enzyme is constitutive (part of the normal enzyme complement of a cell) and present at relatively constant concentrations, whereas COX-2 is inducible and concentrations increase in response to a stimulus. Cyclooxygenase-1 produces PGs that have a cytoprotective function in tissues such as gastric mucosa, kidneys, reproductive tract, and CNS. Similarly, production of thromboxane in platelets is a COX-1 mediated process. Until recently, NSAIDs were believed to have exerted their therapeutically beneficial effects primarily by inhibiting COX-2, whereas drugs that inhibit COX-1 was responsible for some of the toxic side effects, such as gastric ulceration, renal papillary damage, and extended clotting time (Nolan, 2000). Consequently, there has been a shift in focus to drugs that inhibit COX-2 (Livingston, 2000). However, it appears that COX-1 contributes to the inflammatory process and that COX-2 selective inhibitors may not be as efficacious as mixed inhibitors in their antiinflammatory actions. Both COX-1 and COX-2 are constitutively expressed in the CNS and their relative expression varies depending on species (Nolan, 2000). Renal perfusion in hypovolemia is supported by PGs, but studies indicate that both COX-1 and COX-2 are present in kidneys of some species (Livingston, 2000). Gastrointestinal ulceration and hemorrhage, nephrotoxicosis, hepatotoxicity, and decreased platelet function are major side effects associated with NSAID use (Perkowski and Wetmore, 2006).

In mammals, ketamine is a dissociative anesthetic and is an *N*-methyl-D-aspartate (NMDA) glutamate receptor antagonist (Lamont, Tranquilli, and Mathews, 2000). Ketamine produces profound somatic analgesia, but provides little relief of visceral pain (Haskins, Peiffer, and Stowe, 1975). Possible mechanisms of action for ketamine analgesia include depression of spinoreticular tracts (Sparkes et al., 1975), medial medullary reticular formation (Ohtani et al., 1979), and spinal cord lamina (Kitahata, Taub, and Kosaka, 1973), as well as interactions with the CNS and spinal cord opioid receptors (Finck and Ngai, 1982) and NMDA receptor antagonism (Winters, Ferrer-Allado, and Guzman-Flores, 1972).

Analgesic Choice

In mammals, opioids and α_2 -agonists are often chosen for acute, sharp pain, and NSAIDs are often administered for inflammation and chronic pain (Wright, Marcella, and Woodson, 1985). However, NSAIDs also may be used effectively for postoperative pain (Livingston, 2000). Duration, severity, and type of injury and quality of pain dictate the type of analgesia required meet the patient's needs. Species other than mammals can likely use the same groups of analgesics for similar reasons. However, it must be remembered that what might provide analgesia in one species may not in another. The same is true of dose; there are huge variations in effective dosages among species.

SPECIFIC NOTES ON ANALGESIA BY PHYLA

Cephalopods

Cephalopods include octopuses, squid, cuttlefish, and nautiluses. Cephalopods have the most advanced brains and sense organs of all invertebrates and a correspondingly sophisticated behavior (Agnisola, Castaldo, and Fiorito, 1996). The ability of octopuses to use information derived from other observed conspecifics in visual discrimination tasks (Biederman and Davey, 1993) has raised fundamental questions about their cognitive abilities and also suggests that this level of consciousness would allow them to not only perceive pain but also experience it. Given the importance that humans traditionally have placed on pain perception in invertebrates, it is not surprising that there is no emphasis on prevention or treatment pain in cephalopods. There are a few scant papers that have used various methods of anesthesia in cephalopods (Bower et al., 1999) but none described analgesia. Use of electric shock or hypothermia (cold water anesthesia) should not be considered analgesic in cephalopods. Cooling of fish (Jolly, Mawdesley-Thomas, and Bucke, 1972) and reptiles (Calderwood, 1992) to immobilize them may have similar effects. Rapid cooling may in itself be painful (Schumacher, 1996) and lower temperatures have been associated with necrotic changes in the brain of snakes and tortoises (Bennet, 1991). Thus, painful procedures

performed during hypothermic immobilization must be questioned also.

Fish

Sensory Physiology Fish respond to sensory signals such as chemical, hydrodynamic, acoustic, thermal, electrical, light, and mechanical stimuli. Physical changes in heat flow or touch are recognized by skin receptors. Fish display clinical signs of acute and chronic stress and they also exhibit reflexive responses to painful stimuli with strong muscular and behavioral avoidance, and rapid respiration (Brown, 1993). Response to chronic stimuli, including severe wounds, may be not be obvious because conventional behavioral criteria used to identify chronic pain in mammals (e.g., anorexia, recumbency) are not present in fish. Instead, fish may react to chronic stimuli with color changes or less obvious changes in posture and water column use (Stoskopf, 1994). However, the question of central processing of pain by fish remains unanswered and controversial (Stevens, 1992; Rose, 2002; Chandroo, Duncan, and Moccia, 2004; Conte, 2004; Sømme, 2005; Duncan, 2006).

Elasmobranch fish possess fewer unmyelinated nerve fibers than mammals. In long-tailed stingray (Himantua sp.) and large shovelnose rays (Rhinobatus battilum) less than 1% of dorsal root axons are unmyelinated. In smaller shovelnose rays and small black-tipped sharks (Carcharhinus melanopterus), 14% to 38% of axons are unmyelinated. Unmyelinated fibers in these elasmobranchs differ from mammalian nerves in that there is a one-to-one association of the fiber with a Schwann cell. Myelination is incomplete in black-tipped sharks and smaller specimens of the shovelnose ray. Distribution of the diameter of cells of the dorsal root ganglia of the species studied is unimodal, resembling the diameter range that has been reported for somata of myelinated fibers in cats (Simantov et al., 1976). The authors interpret these results as indications that sharks and rays lack the neural apparatus essential for pain sensation and suggest that perception of pain might have little relevance to survival in these species. However, to my knowledge there have been no investigations addressing pain response of elasmobranchs to mechanical, chemical, or thermal stimuli and this should be undertaken before making such a conclusion.

Biochemical evidence for pain perception in fish exists. In teleost (bony fish), there is phylogenetic conservation of high-affinity benzodiazepine-binding proteins similar to alpha subunits of the GABA/benzodiazepine receptor in mammals. Although the same receptors are not found in elasmobranch (sharks and rays) fish, they do have lower affinity sites (Friedl et al., 1988). Substance P-like immunoreactivity, in similar distribution to that reported for other vertebrates, has been identified in gymnotiform fish brain (*Apteronotus leptorhynchus*) and could be related to nociception (Cameron, Plenderleith, and Snow, 1990; Weld and

Maler, 1992). Substance-P immunoreactive substances are associated with afferent nerves sensitive to mechanical stimulation (Ritchie and Leonard, 1983). The presence of these receptors argues for biochemical mediation of pain in ways similar to mammals.

Opioid receptors have been cloned in bony fish (Darlison et al., 1997). In mammals, function of opioid receptors is to modulate pain and the presence of an endogenous opioid system in lower vertebrates may be evidence of central processing modulation of noxious information. Enkephalin activity and associated opiate receptors have been demonstrated in several species of fish, including hagfish, dogfish, shark, carp, salmon, and grouper (Simantov et al., 1976; Olson et al., 1978; Hon and Ng, 1986; Ng et al., 1986; Ng and Chan, 1990). Properties of enkephalin appear similar to other vertebrates and β -endorphins also have been found in salmon (Kawauchi, 1983). Opioid receptors must either function in a similar manner in lower vertebrates or the antinociceptive function evolved later, during evolution.

Cod (*Morhua marisalbi*) and rainbow trout (*Salmo mykiss*) have been shown to respond to painful stimuli and sensitive nociceptive zones have been identified also. In addition, stress decreases nociceptive responses significantly in these fish. Goldfish show appropriate avoidance response (agitated swimming) to an electric shock delivered caudal to the dorsal fin, and incremental doses of morphine produced an increase in the voltage required to elicit a response (Jansen and Greene, 1970). The presence of a substance P-like compound, enkephalin, and opiate receptors support the contrary opinion that elasmobranchs likely experience pain. Structures described may represent a very primitive nociceptive system. Clearly more research is warranted to answer this unresolved question.

Potential Analgesics Lack of data on how and if fish respond to pain make treatment of potentially painful conditions or procedures difficult, but until there is clear understanding we should give fish the benefit of the doubt. All estimations of analgesic efficacy of specific drugs in fish remain anecdotal. Common anesthetics used for fish such as benzocaine and tricaine methanesulfonate (MS-222) have a mechanism of action similar to local anesthetics, which function by preventing transient increases in sodium ion permeability, thereby blocking impulse conduction of nervous tissues (Brown, 1993). Lidocaine in combination with bicarbonate has been used as a general anesthetic, and because it blocks nerve impulses it will likely provide analgesia (Carrasco, Sumano, and Navarro-Fierro, 1984). Recovery from some anesthetics requires drug removal by immersion in fresh water rather than metabolism. Thus, any analgesia the drug provided may be removed also. Ketamine has been used in fish (Williams, Christiansen, and Nygren, 1988), but the mechanism is unknown.

Amphibians

Amphibians have four distinct afferent fiber populations within the dermis corresponding to four distinct sensory modalities. Briefly, the largest and mediumsized axons are rapidly conducting fibers, probably analogous to A β fibers in mammals, that transmit nonnoxious mechanical stimuli (Adrian, 1926; Willenbring and Stevens, 1996). Smaller myelinated axons respond to thermal stimulation, whereas the smallest unmyelinated axons respond to painful stimulation (Maruhashi and Tasaki, 1952). These unmyelinated fibers are likely analogous to the thinly myelinated A δ and unmyelinated C-fibers in mammals that transmit pain.

Peripheral Sensitization Tissue Injury (i.e., light skin scraping) may sensitize frog skin to tactile stimuli. Large fiber firing decreases, whereas slow fiber discharge increases in response to stimuli (Echlin and Propper, 1937). In addition, slowly adapting mechanoreceptors as well as pain receptors respond to noxious stimulation. Recruitment of adjacent nerves has been demonstrated also (Habgood, 1950). Administration of appropriate analgesics prior to a painful stimulus may help to prevent sensitization.

Endogenous Opioid System As in mammals, endogenous opioid systems modulate central processing of noxious information in amphibians (Lorez and Kemali, 1981; Stevens, 1988). Amphibians possess a welldeveloped endogenous opioid system (Doerr-Schott, Dubois, and Lichte, 1981) and spinal administration of endogenous opioids (i.e. dynorphin, β-endorphin or Met-enkephalin) produces a potent, dose-dependent increase in nociceptive threshold in unanesthetized frogs (Pezalla and Stevens, 1984) that can be blocked effectively with naloxone (Stevens, Sangha, and Ogg, 1995). Analgesia can be altered by stressful conditions such as handling and unfamiliar housing conditions (De Kock and Meert, 1997). Stress caused by restraint produces naloxone-reversible analgesia in frogs (Pezalla, 1983; Stevens, Sangha, and Ogg, 1995), indicating endogenous release of opioids. However, analgesia in response to combined stresses of restraint and transfer to an unfamiliar environment may result in analgesia that can not be blocked by naloxone and thus involves a non-opioid pathway (Pezalla, 1983). Although stress may produce analgesia in some situations, stress alone should not be considered necessary or sufficient to induce analgesia (Stoskopf, 1994).

In frogs, endogenous opioid systems are reduced during hibernation. Cold-adapted frogs show a significant decrease in nociceptive threshold and an increase in pain sensitivity compared with frogs kept at room temperature. In addition, cold-adapted frogs returned to room temperature show a naloxone-reversible increase in nociceptive threshold (Stevens and Pezalla, 1989). In a more recent study, regional hypothermia (hind limb

with a tourniquet) provided analgesia that was mediated, in part, by opioid compounds. However, this analgesia was only blocked partially by opioid antagonists, suggesting that mechanisms other than the opioid system also may be involved (Suckow et al., 1999). In addition, after warming, any potential analgesic benefits that may have arisen from hypothermia disappeared. Hypothermia may produce analgesia in some situations (Suckow et al., 1999), but in other situations it may result in decreased nociceptive threshold (Stevens and Pezalla, 1989). Therefore, it should not be assumed that hypothermia (Parker, 1939) produces sufficient analgesia to perform any procedure that would be considered painful in other animals (Morton and Griffiths, 1986).

Opioids Early studies failed to detect opioid analgesia in amphibians using the hotplate test or electrical shock procedures, as used commonly in mammals. However, a potent analgesic effect of morphine using the acetic acid test has been demonstrated (Pezalla, 1983). Application of acetic acid to the frog's hind leg produces a spinally mediated wiping reflex, which is reproducible and used for nociceptive testing in most pain experiments involving amphibians (Pezalla, 1983). Direct administration of opioids to frog spinal cord produces potent, dosedependent, reversible analgesia that is blocked completely by pretreatment with naloxone (Pezalla, 1983) or naltrexone (Stevens, Klopp, and Facello, 1994; Stevens, 1996; Willenbring and Stevens, 1996; Stevens and Rothe, 1997).

In comparison with mammals, analgesia produced by morphine (10 to 100 mg/kg) has little effect on motor reflexes, feeding, or general behavior of amphibians. Higher doses of morphine (320 to 640 mg/kg) cause hyperresponsiveness to sensory input similar to the high-dose response in cats (Pezalla, 1983). Amphibians also develop opioid tolerance to repeated systemic morphine injections, as seen by both a decrement in drug effect over time and a significant shifting to the right of morphine dose-response curves in tolerant animals (Stevens and Kirkendall, 1993; Stevens, Klopp, and Facello, 1994).

The pharmacokinetics of systemic opioids differs between amphibians and mammals. In amphibians, all μ -agonists appear to produce a gradual increase in effect during the first hour after administration and reach peak analgesia by 60 to 90 minutes (Stevens, Klopp, and Facello, 1994). In contrast, similar studies in rodents indicate drug lipophilicity and onset is correlated significantly (Kutter et al., 1970). Compared with mammals, blood flow in and out of the CNS is lower in amphibians and may contribute to delayed opioid action onset and longer duration of analgesia (Stevens, Klopp, and Facello, 1994). Amphibians have reduced capacity for hepatic metabolism, which may suggest that metabolism of opioids is slower than in other species (Gorge, Beyer, and Urich, 1987). Amphibians appear to require

greater doses of systemic opioids to produce analysia compared with rodents, although algesiometric tests differ (Stevens, Klopp, and Facello, 1994).

 α_2 -Agonists As with endogenous opioid systems (Stevens, 1992), mammals and amphibians may share common anatomical and functional characteristics in α₂-adrenoceptor-mediated analgesia (Willenbring and Stevens, 1996). Duration of effect is altered by location as analgesia lasted 6 to 8 hours (Brenner et al., 1994) with subcutaneous administration and 4 hours with intraspinal administration (Stevens and Brenner, 1996). Systemic adrenergic agonists produce analgesia in amphibians with a similar order of potency to that reported in mammalian studies (Brenner et al., 1994). Dose-dependent sedation is seen in mammals (Doze, Chen, and Maze, 1989), whereas doses of 10 mg/kg dexmedetomidine or clonidine in frogs do not produce sedation as animals retain corneal, righting and hind limb withdrawal reflexes (Brenner et al., 1994). Although other α_2 -agonists, such as xylazine, also have antinociceptive properties (Luttinger et al., 1985), efficacy in amphibians has not been demonstrated.

Tricaine Methanesulfonate, Local Anesthesia, and **Ketamine** Tricaine methanesulfonate can be administered to amphibians by immersion, or by intracelomic, intramuscular, or subcutaneous injection (Letcher and Amsel, 1989; Letcher, 1992). Intraspecies and interspecies variation in effect may be important, and this agent should be used cautiously in unfamiliar species (Letcher, 1992). Tricaine and local anesthetics may potentially be used for control of pain in lower vertebrates during surgical procedures, as they block neural transmission (Stoskopf, 1994). Recovery from tricaine involves removal of the drug by placing the animal in a water bath to wash the drug away; it is important to keep in mind that this procedure will also remove any existing analgesia. In amphibians, mode of action of ketamine may be partially mediated through opioid receptors (Lee and Frank, 1991), and thus may potentially provide some somatic analgesia.

Reptiles

Few studies have investigated mechanisms of pain regulation and effects of analgesic drugs in reptiles (Read, 2004). Pain-related behavior has been demonstrated in a number of species. Acute pain in reptiles is characterized by withdrawal of a limb (Kanui and Hole, 1992; Chrisman et al., 1997), escape or avoidance response (Kanui and Hole, 1992), and attempts to bite (Stoskopf, 1994). Rapidly adapting mechanoreceptors have been identified in the carapace and plastron of tortoises. Sensitive areas are concentrated on the perimeters of the scutes. Receptors respond more to transient (acute) stimuli rather than steady pressure (Rosenberg, 1986). Tortoises have capacity to locate accurately a tactile

stimulus applied to the shell (Stein and Grossman, 1980; Rosenberg, 1986) and respond in a reflex manner by scratching (rubbing the foot against the stimulated area) (Stein and Grossman, 1980). However, it is unclear if nociception is involved in this reflex.

Primary Aδ nociceptive neurons have been identified in the oral mucosa and facial skin of the snake. Reptiles have a similar gross and histological arrangement of the spinal cord compared with mammals, and nociceptive neurons identified were very similar to those identified in monkeys (Liang and Terashima, 1993). As in fish and amphibians, reptiles possess an endogenous opioid system (Ng et al., 1986). Enkephalin content in turtle brain is greater than that in mammals (Simantov et al., 1976). Crocodiles are sensitive to low doses of opioids and develop significant latencies in response to a painful stimulus (hot plate, and capsaicin instillation tests) after injection of pethidine (1 to 8 mg/kg, maximal effect at 2 to 4 mg/kg) and morphine (0.1 to 1.0 mg/kg, maximal effect at 0.3 mg/kg) (Kanui, Hole, and Miaron, 1990; Kanui and Hole, 1992). Both drugs demonstrated a dosedependent response that reached a plateau (Kanui and Hole, 1992). Anoles demonstrate a latency of the tailflick response when administered morphine (5 mg/kg) (Mauk et al., 1981). Butorphanol (1 mg/kg) in iguanas does appear to produce any isoflurane-sparing effects (Mosley, Dyson, and Smith, 2003).

Neuromuscular blocking agents have been used commonly for immobilization of reptiles (Brazenor and Kaye, 1965; Brisbin, 1966; Morgan-Davies, 1980). These agents can be categorized as depolarizing (i.e., succinylcholine chloride, decamethonium iodide) and nondepolarizing (i.e., atracurium besylate, gallamine triethiodide, D-tubocurarine chloride). Immobilization results in paralysis of the animal without analgesia or unconsciousness (National Research Council Committee, 1992). Therefore, any procedure done using these agents alone must be considered inhumane. Electroanesthesia is another form of paralysis that uses a low- to high-frequency sine wave ratio of 25% to induce and maintain "anesthesia" for surgery (laparotomy and leg amputation) in iguana (Nothway, 1969). It is unknown if this procedure affects consciousness or provides any pain relief; therefore, analgesia must be provided.

Local anesthetic (i.e., 2% lidocaine and 1% procaine) infiltration, blocking neurotransmission of a painful stimulus, has been used to provide analgesia for minor procedures (abscess removal and skin lacerations) in conscious animals (Marcus, 1981; Bennet, 1991, 1998).

Birds

Sensory Physiology Birds possess the neurological components to respond appropriately to a painful stimulus. They have endogenous antinociceptive mechanisms to modulate pain, and treatment with pharmacological agents used in mammals modulates pain

pathways and behavioral responses to painful stimuli (Gentle, 1992; Machin, 2005). Birds have three types of nociceptors: high threshold mechano-thermal, mechanical, and thermal nociceptors. Mechano-thermal nociceptors are polymodal pain receptors because they have more than one function (Gentle, 1992). They respond to temperatures above 40°C and mechanical stimulation and they have been identified in pigeons (Necker and Reiner, 1980), waterfowl (Gottschaldt, Fruhstorfer, and Schmidt, 1982), and chickens (Gentle, 1992). Conduction of impulses is slow and they are comparable to mammalian unmyelinated C-fibers arising from cutaneous free-nerve endings that transmit pain. Increasing magnitude of stimulus results in an increase in responses. Some fibers show continuous response up to the highest temperature tested (56°C), whereas other fibers show a clear peak in response at a lower temperature, and increasing stimulus intensity beyond this temperature results in a reduced response (Gentle, 1991).

Endogenous opioid systems appear to modulate central processing in birds (Reiner, Davis, and Brecha, 1984). Birds possess μ -, κ -, and δ -opioid receptors in similar proportions as seen in humans (Danbury, Hudson, and Waterman-Pearson, 1998). Opioid receptors are detectable in 10-day-old chick embryos and are concentrated in areas thought to play key roles in sensory input processing and memory (Hendrickson and Lin, 1980). Within the avian telencephalon, distribution of β-endorphin and enkephalin-like immunoreactivity, is similar to the mammalian telencephalon (Wan and Pang, 1994), indicating that binding sites are similar. Evidence demonstrates that the endogenous opioid system plays an important role in pain modulation and perception because male broiler chickens with degenerative joint disease affecting the hip walked more slowly when they were given an injection of naloxone (an opioid antagonist) (Hocking, Bernard, and Maxwell, 1999).

Pain-Associated Behavior Although there are no reliable or universal indicators of pain, birds tend to respond to noxious stimuli with a fight-flight response (escape reactions, vocalizations, and excessive movement) (Gentle and Hunter, 1990) and/or conservationwithdrawal responses (no escape attempts vocalizations and immobility) (Woolley and Gentle, 1987; Gentle, 1992). In chickens, acute pain (such as feather removal) is usually characterized by wing flapping and/or vocalization and by decreased head movements, increased heart and respiratory rates, and increased blood pressure (Gentle and Hunter, 1990). Electric shock or comb pinch, also producing acute pain, results in active avoidance behavior involving vigorous escape attempts (jumping and wing flapping) with some vocalization (Paul-Murphy, Brunson, and Miletic, 1999). In comparison, inappetence, inactivity and "puffed-up" appearance are often demonstrated when birds are exposed to prolonged pain (Gentle and Hunter, 1993).

Prolonged pain by continual feather removal tends not to produce an exaggerated escape response; instead birds crouch in an immobile state. Changes in blood pressure and electroencephalograph arousal immediately after feather removal suggest that pain sensation is present (Gentle, Jones, and Woolley, 1989).

In addition to behavioral evidence, anatomical and physiological evidence supports chronic pain following partial beak amputation. Adjacent to the scar tissue, damaged and regenerating nerve fibers formed extensive neuromas (Breward and Gentle, 1985). Electrophysiological recordings from nerve fibers innervating these neuromas are abnormal for trigeminal afferent fibers. The most characteristic abnormality was the presence of abnormal spontaneous neural activity in the trigeminal nerve from the beak stump 5 to 83 days after initial amputation (Breward and Gentle, 1985). Neural activity arising from trigeminal neuromas was similar to that reported in experimental neuromas in rat, mouse, and cat. Studies on peripheral nerve injury and subsequent neuroma formation in mammals have suggested that abnormal activity from regenerating axons is implicated in post-amputation stump pain (Breward and Gentle, 1985).

Response to noxious stimuli can vary greatly from species to species. Electric shock and thermal tests have been used effectively in gallinaceous birds but one study in conscious parrots (African gray parrots *Psittacus erithacus erithacus* and *P. erithacus timneh*) found that large variation among responses prevented meaningful quantitative assessment of temperature threshold (Paul-Murphy, Brunson, and Miletic, 1999). In comparison, it was possible to identify when some African grays became aware of the electrical stimulus, because they would look down at their foot or chew on the wire. The amount of stimulus that caused the bird to lift its foot could be measured reliably and response was attenuated with opioids (Paul-Murphy, Brunson, and Miletic, 1999).

Potential Analgesics

Opioid Analgesics Opioids can be used effectively in avian species, but reports in the literature show variable and conflicting results (Bardo and Hughes, 1978; Curro, Brunson, and Paul-Murphy, 1994; Concannon, Dodam, and Hellyer, 1995; Paul-Murphy, Brunson, and Miletic, 1999). Clinical use of opioids in avian species has been hindered also by lack of published information and possible differences in opioid actions between avian and mammalian species, and even among different species of birds. Differences in response to opioid analgesics may be related to the proportion of opioid receptor subclasses present in different species (Clyde and Paul-Murphy, 1999). Different distributions of opioid receptors in birds may account for differences in response to opioids between mammals and birds (Hoppes et al., 2003). Autoradiographic studies of pigeon fore-brains show a predominance of μ-receptors in comparison

with mammals but both ∞ - and κ -agonists are capable of producing analgesia (Herling et al., 1980).

Buprenorphine is a partial agonist that binds readily to μ -receptors and has some κ -antagonist properties. Being a partial agonist, it does not induce the same degree of effect as a full agonist, such as morphine, and is only effective for treating mild to moderate pain. Buprenorphine (0.01 to 0.05 mg/kg) has been reported to be clinically effective in birds (Clyde, 1994; Beynon, 1996) but in African gray parrots, large doses (0.1 mg/kg) produced no significant analgesic effect (Clyde and Paul-Murphy, 1999; Paul-Murphy, Brunson, and Miletic, 1999). In a more recent study, buprenorphine administered IM at 0.1 mg/kg failed to reach plasma levels that would be considered analgesic in humans (Paul-Murphy, Hess, and Fialkowski, 2004).

Butorphanol is a weak antagonist at the μ-receptor, but a strong agonist at the κ-receptor used commonly in small and large animal anesthesia for premedication and analgesia. In mammals, butorphanol produces analgesia in a dose-dependent manner with fewer respiratory depressant effects compared with morphine. In parrots, addition of butorphanol (1 mg/kg) to isoflurane decreased isoflurane required during application of a painful stimulus (termed isoflurane-sparing effect) or reduction in MAC cockatoos by 25% and 11% in African gray parrots but did not change significantly in bluefronted Amazon parrots (Curro, 1994; Curro, Brunson, and Paul-Murphy, 1994). However, care should be taken when interpreting this kind of information as isoflurane-sparing can be accomplished through sedation rather than analgesia (Dohoo, 1990). Another study was unable to demonstrate a reduction in the amount of halothane required to anesthetize turkeys during surgery with the addition of butorphanol (0.1 mg/kg), but birds treated with but orphanol had fewer responses to noxious stimuli than did controls (Reim and Middleton, 1995). Butorphanol (1.0 mg/kg) significantly increased threshold to electrical stimuli in half of the conscious African gray parrots tested (Paul-Murphy, Brunson, and Miletic, 1999).

Fentanyl is a μ -receptor agonist and is used in mammals for relief of severe pain. Concentrations considered to be analgesic in humans was achieved in white cockatoos and maintained for at least 2 hours with a dose of 0.02 mg/kg IM. However, no significant difference was found in analgesic response between birds given saline and those given fentanyl. However, a dose of 0.2 mg/kg subcutaneously did provide significant analgesia in some birds. In addition, the authors do not recommend fentanyl at this dose routinely because of the large volume of drug that must be injected and the consequent hyperactivity seen in some birds (Hoppes et al., 2003).

Steroidal Anti-inflammatory Drugs (Corticosteroids) Corticosteroids may reduce pain by suppressing response to chemical, thermal, traumatic, or inflammatory injury

through reduction in fibroblast proliferation, macrophage response to migration inhibition factor, sensitization of lymphocytes, and response to mediators of inflammation. Combination of long-acting local anesthetic agents (i.e., bupivacaine) and corticosteroids has been shown to reduce postoperative discomfort in humans (Glasser et al., 1993). Betamethasone is a powerful steroidal antiinflammatory drug that reduces pain associated with degenerative hip disorders in adult male turkeys (0.1 mg/kg) (Duncan et al., 1991). Intraarticular injection of sodium urate produces acute synovitis with inflammatory changes such as swelling, increased joint temperature, and sensitization of the joint capsule receptors lasting at least 3 hours. In this model in chickens, betamethasone decreased inflammation (Hocking, Bernard, and Maxwell, 1999) and betamethasone (0.04 mg/kg), dexamethasone (0.06 mg/kg), and methylprednisolone (2 mg/kg) decreased pain related behavior (Hocking, Robertson, and Gentle, 2001).

Risk of possible immunosuppression and other potential complications make NSAIDs preferable in many situations (Clyde and Paul-Murphy, 1999).

Nonsteroidal Antiinflammatory Drugs Prostaglandins are involved in modulation of avian pain responses and physiological mechanisms involving PGs are similar to that described in mammalian models (Nicol, Klingberg, and Vasko, 1992). Pharmacokinetic studies on oral NSAID administration show a shorter half-life and lower bioavailability compared with mammals. Unfortunately, pharmacokinetic data cannot be extrapolated between species (Nolan, 2000) and pharmacokinetic studies of NSAIDs are poor predictors of analgesic efficacy (Roder et al., 1999). Plasma levels do not reflect physiological or pharmacological activity because they are weak acids, highly protein bound, and tend to accumulate in areas of inflammation (Lees et al., 1987). Physiological actions of drugs can be used to gain information about how NSAIDs function within the animal. For example, NSAIDs block access of arachidonic acid to its binding site on the COX enzyme, thus preventing conversion to thromboxane B₂ (TBX). Consequently, TBX may be used to estimate the length of NSAID action. In mallard ducks, flunixin meglumine (5 mg/kg) and ketoprofen (5 mg/kg) suppressed TBX levels for up to 12 hours, possibly suggesting that their physiological action may be that long (Machin, Tellier, and Lair, 2001), but further studies are necessary to confirm length of analgesia.

Preemptive use of NSAIDs may decrease tissue sensitization caused by surgical trauma and may reduce the amount of postoperative opioids needed. They can be used effectively in the postoperative period in both mammalian and avian patients. Both sodium salicylate and acetaminophen have analgesic properties in pigeons (Brune, Bucher, and Waltz, 1974). Indomethacin has been shown to have antiinflammatory effects in the chicken (Ito and Bohn, 1986) and analgesic effects in

pigeons (Benzi, Crema, and Frigo, 1966). Chickens undergoing a partial beak amputation given phenylbutazone topically were able to maintain their pretrimming feed intake levels over the first 24 hours after the procedure (Glatz, Murphy, and Preston, 1992), and this was higher than in untreated birds. Chickens given a 1 mg/kg subcutaneous dose of carprofen had peak plasma levels 1 to 2 hours after injection and raised pressure thresholds (decreased response to pressure) for at least 90 minutes after a subcutaneous injection. Lame chickens preferentially select food with carprofen compared with food without analgesics and amount of carprofen consumed increased with severity of lameness (Danbury, Chambers, and Weeks, 1997). In another study, carprofen increased speed and walking ability of rapidly growing broiler chickens with chronic lameness (McGeown et al., 1999). Minimum effective doses for producing analgesia in an intraarticular injection of sodium urate model in chickens for carprofen, flunixin, and ketoprofen, respectively, were 30, 3, and 12 mg/kg (Hocking, Robertson, and Gentle, 2001).

Administration of ketoprofen (5 mg/kg) reduced increases in heart and respiratory rates associated with application of a noxious stimulus in spontaneously breathing adult female Mallard ducks anesthetized with isoflurane. In addition, the mean time a noxious stimulus could be applied before gross purposeful movements were seen (up to a maximum of 5 seconds) was significantly longer when ducks were given ketoprofen than when they were given saline solution. Administration of ketoprofen at a dose of 5 mg/kg to Mallard ducks results in clinically detectable analgesia (Machin and Livingston, 2002).

Nonsteroidal antiinflammatory drugs are capable of producing gastrointestinal ulceration and bleeding because of inhibition of PG synthesis. Similarly, regurgitation and tenesmus has also been noted in budgerigars when a high dosage of flunixin (10 mg/kg) was given (Clyde and Paul-Murphy, 1999). Nephrotoxicity has been reported with the use of flunixin in northern bobwhite and in different species of mammals (Klein, Charmatz, and Langenberg, 1994). Renal ischemia and necrosis has been documented in Siberian cranes (Clyde and Paul-Murphy, 1999) and anecdotal reports also suggest that the repetitive use of flunixin can cause lesions of renal gout in different species of birds (Klein, Charmatz, and Langenberg, 1994). Muscular necrosis at the site of injection has been documented in mallard ducks (Machin, Tellier, and Lair, 2001), and northern bobwhites (Klein, Charmatz, and Langenberg, 1994). Flunixin meglumine appears to produce more adverse effects in birds than other NSAIDs (Clyde and Paul-Murphy, 1999).

A combination of bupivacaine and ketoprofen during propofol anesthesia resulted in mortality of male spectacled and king eiders. Death of the male eiders was likely caused by renal damage induced by ketoprofen.

They were predisposed to chemical injury because of the behavioral and physiological differences between male and female eiders. The potential interaction of the three drugs in male eiders is not clear (Mulcahy, Tuomi, and Larsen, 2003).

More recently meloxicam at 0.1 mg/kg has been suggested for use in avian species (Paul-Murphy and Ludders, 2001); however, there are no published reports of its efficacy for pain management or safety in avian species. Variation in pharmacokinetics data does not allow dosage extrapolation between species (Nolan, 2000). For example, elimination half-life of meloxicam in dogs is 24 hours (Poulsen-Nautrup and Hoerstermann, 2003) compared with 4 hours in the minipig and 11 hours in the rat. Similarly, ostriches administered 0.5 mg/kg meloxicam exhibited a very rapid half-life when compared with ducks, pigeons, and chickens. Half-life of the drug seems inversely proportional to the bird's weight, with smaller birds needing less dosing and larger birds needing perhaps increased dosing intervals. No adverse effects were noted at 0.5 mg/kg in two pharmacokinetic studies (Baert and De Backer, 2002a,b), but no analgesic efficacy data were obtained.

 α_2 -Adrenergic Agonists Like mammals, avian sensitivity to noxious stimuli is susceptible to adrenergic modulation. Although inclusion of α_2 -agonists (such as xylazine and medetomidine) can be useful in premedication for balanced anesthesia during painful procedures, postoperative administration of α_2 -agonists is not usually used in birds because of undesired effects. They can produce muscle tremors, respiratory depression, and birds still move in response to noise (Redig, 1982). Other disadvantages of α₂-agonists include hypertension following IV bolus injections, hypotension, bradycardia with partial A-V block (Virtanen, 1989), dose-dependent hypothermia by decreasing thermogenesis, increased postoperative fluid requirements, sedation, and respiratory depression. To reduce negative effects, they are often combined with other drugs, such as ketamine. Atipamezole is a highly potent, specific, competitive α_2 -antagonist of centrally and peripherally located α_2 -adrenoceptors that will quickly relieve any unwanted side effects, but administration also reverses analgesia (Virtanen, 1989).

Ketamine Ketamine is often combined with sedatives such as α_2 -agonists and benzodiazepines for premedication or general anesthesia for minor procedures in birds. Low-dose ketamine can be useful for preemptive analgesia in major surgeries and also for postoperative analgesia, as it can enhance analgesia by preventing or abolishing NMDA receptor-mediated sensitization in the CNS. Although ketamine prevents sharp, superficial pain effectively, it does not control visceral, dull pain, so ketamine alone is not adequate for laparotomies or orthopedic surgery (Lamont, Tranquilli, and Mathews, 2000).

Local Anesthetics Local anesthetics are effective for pain control or prevention of pain in avian species. In domestic fowl, bupivacaine produces effective analgesia in two pain models. Chickens that had topical bupivacaine applied to the beak stump after amputation were able to maintain their pretrimming feed intake levels over the first 4 hours after the procedure (Glatz, Murphy, and Preston, 1992). In uric acid-induced hock-joint pain, intraarticular bupivacaine (2 mg/kg) increased feeding, pecking, and standing behaviors, whereas the proportion of resting declined and was indistinguishable from animals in the control group (Hocking et al., 1997).

Duration of local anesthetics action in avian species is unknown. In mammals, lidocaine is a shorter acting (60 to 120 minutes) compared with bupivacaine (240 to 360 minutes) (Skarda, 1996). A pharmacokinetic study of a single dose (2 mg/kg) of bupivacaine in mallard ducks suggests that it may be shorter-acting than it is in mammals (Machin and Livingston, 2001).

Birds may be more sensitive to the toxic effects of local anesthetics than mammals, as lower doses in birds (2.7 to 3.3 mg/kg) produce toxic effects (Hocking et al., 1997) compared with higher doses (3.5 to 4.5 mg/kg) in dogs (Skarda, 1996). It is recommended that lidocaine dose not exceed 4 mg/kg in birds because seizures and cardiac arrest can be produced with overdose. Chickens receiving higher doses of bupivacaine (2.7 to 3.3 mg/kg) showed signs of toxicity (recumbency with outstretched legs, drowsiness) and distress immediately after injection (Hocking et al., 1997). Pharmacokinetics suggests that absorption of bupivacaine is shorter than elimination, which may, in part, explain why birds are susceptible to toxic effects of local anesthetics. In addition, the appearance of high levels of plasma bupivacaine 6 to 12 hours after administration may contribute to the apparent avian sensitivity to toxic effects of local anesthetics (Machin and Livingston, 2001). Pharmacokinetics may contribute to the sensitivity of avian species to local anesthetics, but other possible mechanisms could be involved. The avian blood-brain barrier is not as complex as that of mammals (Stewart and Wiley, 1981), and this may allow for higher concentrations of local anesthetic in the brain. More studies are necessary to elucidate the mechanism of local anesthetic toxicity in avian species. Other adverse side effects of local anesthesia include depression, drowsiness, ataxia, nystagmus, muscle tremors, and possibly hypotension (Hocking, Bernard, and Maxwell, 1999). Bupivacaine dose should not exceed 2 mg/kg.

Anesthesia of any animal, including birds, may not necessarily induce appropriate analgesia. Most birds are anesthetized solely with an inhaled anesthetic, frequently isoflurane or sevoflurane. During volatile anesthesia, the CNS is depressed sufficiently to prevent the perception of pain but the anesthetic does not necessarily provide analgesia (Dohoo, 1990). In fact, all inhaled

anesthetics can be hyperalgesic (produce extreme sensitivity to pain) at very low concentrations (i.e., concentrations that would be obtained at some point during recovery from anesthesia) by enhancing C-fiber activity (Zhang et al., 2000). Violent recoveries from inhalant anesthesia have been noted in birds when hyperalgesia is also present. It is possible that some of this behavior during recovery may be attributable to intense pain. Provision of appropriate perioperative analgesia may improve recovery in avian species. Although local anesthesia is sufficient for pain relief, it does not reduce stress that may be induced by physical restraint and handling of an awake bird. Sedation or general anesthesia should also be considered during stressful or prolonged procedures.

Mammals

Surprisingly, there is very little information specifically about analgesia in wild mammals. There are many studies of wild species that sometimes include descriptions of painful procedures, yet there is no reference that specifically addresses pain or analgesia of wild mammals. Most often dosages and choice of analgesic agent are extrapolated from the closest similar domestic species. The biggest challenge facing wildlife veterinarians is lack of species specific information related to analgesia. I also encourage readers to refer to other portions of this book for reference to analgesia of different species.

Recognition and Assessment of Pain Although some of this information can be applied to non-mammalian species, the techniques described here are more specific to mammals and therefore discussed within this section. At least three types of response to pain can be recognized: (1) Responses designed to modify the animal's conscious behavior, to enable it to learn and avoid future exposure to painful experiences. These responses result from the aversive quality of the pain. (2) Automatic responses, which are designed to protect the animal or parts of the animal. These include withdrawal from or removal of the stimulus, or attempts to achieve the same result. A withdrawal reflex may a minimal response and an exaggerated response would be to run away. The animal may attack the source of the stimuli or attempt to minimize pain by lying or standing very still or by assuming another posture that helps to do this. (3) Responses that are designed to convey the experience to others of the same species or other species, which may help to alleviate the situation, e.g., pain-specific vocalization, facial expression, posture, etc. Under normal evolutionary selection pressure, in which predators are likely to detect the response, these responses may be suppressed. In some social species, responses are well developed and may elicit help from fellow members of the social group: This is seen in primates (Sanford et al., 1996). These types of responses usually occur simultaneously.

Table 3.1. Suggested dose rates for analgesia in mammals.

	Buprenorphine	Butorphanol	Ketoprofen	Meloxicam
Squirrels and small rodents Bobcat, otter, raccoon, opossum, fox, skunk	0.05 mg/kg IM bid-tid 0.005-0.01 mg/kg IM bid	0.2 mg/kg IM bid-qid 0.2 mg/kg IM bid-qid	1–2 mg/kg IM bid 1–2 mg/kg IM bid	0.1-0.2 mg/kg PO sid 0.1-0.2 mg/kg PO sid
Deer, small ruminants	0.005 mg/kg IM bid	0.2 mg/kg IM bid-qid	1-2 mg/kg IM bid	0.1-0.2 mg/kg PO sid

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Observation can be an important tool for assessing pain and its alleviation if behavior of the animal is understood. If possible the animal should be watched from a distance for signs of abnormal activity (i.e., limping, repetitive licking, kicking or scratching of a particular area, teeth grinding, guarding of an area, etc.), and changes in activity such as sleep-wake patterns, exploratory behavior, eating and foraging behavior, etc. (Sanford et al., 1996). Postural changes, vocalization, and changes in facial expression are used as means of communication in many species. Changes in facial expression in response to pain have not been systematically investigated for animals. Many animals do not seem to wrinkle or furrow their brows, frown, or grimace as shown by humans in pain (Williams, 2002). Longterm care givers of individual animals may recognize subtle differences in facial expression, but they have not been adequately described for use by others.

Objective assessment of pain can be done through evaluation of physiological and biochemical (i.e., adrenocorticotropic hormones) indices and behavior. Behavioral assessment of pain requires intimate knowledge of normal behavior of the species. The ideal pain assessment is simple, accurate, reliable, and sensitive to pain intensity. It should have a ratio scale, be free from bias, and be useful for both experimental and clinical pain. Pain scoring was first developed for human pain assessment. Animal pain scoring is unidimensional and is either on a discontinuous or continuous scoring system. The most common types of scales are discontinuous with several behavioral factors having number gradation. Continuous scales are visual analogue scales (VAS) and used most often in small animal pain assessment. The system uses a 100-mm line continuum with the least pain on one and the worst pain on the other. In human medicine, the subject is asked to mark the spot on the line where he or she would rank the pain experienced. For animal pain, the observer evaluates the pain first by observation and by application of pressure to the affected area. The use of this system has shown good correlation with discontinuous scales. The disadvantages of the VAS are that it assumes that all animals react similarly and all types of pain can be assessed in similar ways (Welsh, Getinby, and Nolan, 1993). Also each species requires different ranking criteria.

Analgesia There is next to no information specifically addressing analgesia in wild animals. A few case reports have assessed analgesia in some captive wildlife species. Most assessment of analgesia in published studies have been during anesthesia and rarely post-handling or postoperatively. If a procedure is known to be painful in other species or humans, then it should be assumed to be painful in the species in question (Morton and Griffiths, 1986). For example, tooth extraction and tissue sampling should be assumed to require analgesia. Local anesthetics are a good choice to provide analgesia both during and after the procedure.

For mammals, epidural administration is an additional option for analgesia that is not used in other phyla. Morphine (0.1 mg/kg) was administered into the epidural space in the lumbosacral region prior to a total hip replacement in a cheetah (*Acinonyx jubatus*). Epidural administration of morphine was chosen because of longer analgesic duration compared with systemic administration (Pablo et al., 1995). Expected analgesic effect in humans is 6 to 24 hours (Behar et al., 1979). Although the cheetah transiently attempted to chew the area, the authors feel that the epidural provided adequate analgesia because of return to normal behavior within 3 hours after anesthesia (Pablo et al., 1995).

Medetomidine (5 μ g/kg) and bupivacaine (0.25 mg/kg) administered epidurally at the lumbosacral space was used for a femoral head and neck excision in a brown bear (*Urusus arctos arctos*). The epidural apparently reduced inhaled anesthetic (isoflurane) requirement by 28% to 44% and provided postoperative pain control for 10 to 14 hours. The bear was also given Meloxicam 0.5 mg/kg subcutaneously once and then 0.1 mg/kg per os (PO) mixed with honey for 2 weeks prior to the surgery, but no comment was made on alleviation of pain while the bear awaited surgery for luxation of the right femoral head (Witz et al., 2001).

One experimental study involving manipulation of the reproductive tract and transvaginal ultrasound-guided oocyte collection in sedated and blindfolded Addax (*Addax nasomaculatus*) used repeated epidural lidocaine (0.17 to 0.38 mg/kg) placed at the sacrococcygeal intervertebral space or first intercoccygeal intervertebral space. Animals were sedated with acepromazine maleate (0.14 to 0.34 mg/kg) with one animal given supplemental xylazine (0.17 mg/kg) to improve sedation. Adequacy

of epidural analgesia was judged by loss of muscular function of the tail, relaxation of the rectum to allow palpation, and relaxation of the vulva to allow ultrasound probe insertion. Analgesia was reported to be excellent in 12 procedures in which the lidocaine average dose was 0.32 mg/kg; fair in six procedures in which the average dose was 0.31 mg/kg; and poor in three procedures in which the average dose was 0.24 mg/kg. Supplemental xylazine sedation did not appear to alter the quality of the epidural analgesia.

Drug dosages for a variety of species are listed in Table 3.1, but to this author's knowledge all of the drugs and dosages listed are anecdotal and efficacy has not been tested. The reader should view these as a place to start and where possible report both positive and negative findings in the form of publications or presentation so that our basic knowledge of analgesia in wild animals will improve.

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4

Remote Drug Delivery

Ramiro Isaza

INTRODUCTION

The ability to effectively and safely administer anesthetic drugs to non-domestic species is one of the central tasks facing practitioners of zoological medicine. Prior to the development of both effective anesthetics and remote delivery systems, veterinary procedures on non-domestic species were either impossible to accomplish or associated with unacceptably high mortality rates. This chapter examines the methods of anesthetic drug delivery with an emphasis on the commercial equipment available to the practitioner.

DIRECT DELIVERY SYSTEMS FOR COOPERATIVE ANIMALS

Restraint Methods

Behavioral Restraint The techniques employed to administer anesthetic drugs to an animal depend largely on whether or not the animal is cooperative during the pre-induction period. It is often assumed that most non-domestic species will be uncooperative and the animal will be either unwilling to accept treatment or it is too dangerous to use traditional routes of drug administration. In contrast, a cooperative animal is one that will allow the veterinarian to perform a routine physical examination or administer medication on a regular basis with minimal restraint.

These animals can be treated like traditional anesthetic patients in whom intramuscular and even intravenous injections can be given. Training an animal to accept injections and manipulation is beneficial to both the animal and the veterinarian. Effective training prior to the procedure reduces the stress associated with anesthesia and increases the likelihood of compliance. An example is training a chimpanzee to place its arm through the cage to receive injections. The most extreme example is seen in well-trained elephants or whales that permit direct manipulation despite their overwhelming size (Figure 4.1).

These animals are usually trained to accept human manipulation, and are well socialized and under voluntary behavioral restraint. In many of these situations, the relationship and trust that a trainer has with the animal should not be underestimated. Often an animal will refuse medication offered by a stranger that will subsequently be accepted if presented by the trainer. Having the anesthetic procedures begin in the animal's regular enclosure with its usual handler will facilitate induction.

When feasible, behavioral restraint is usually less stressful to the animal, but the veterinarian must be aware of the limitations of this situation. Quiet, well-trained animals may become dangerous if placed in unfamiliar environments (e.g., hospitals) or if given unexpected painful stimulations such as injections.

Manual Restraint Manual restraint is typically restricted to individual animals that are assumed, by the handler or veterinarian, to be neither dangerous to handlers or themselves (Figure 4.2).

In order for this assumption to be valid, the restrainer must be very knowledgeable of the species and the likely response by the animal to the proposed treatment (Fowler, 1995). Restraint may be enhanced by the use of thick leather welder's gloves, towels, linen bags, nets, and rabies poles. Once the animal is contained, anesthetic induction agents may be administered. These methods are routinely used with small animals such as raptors, small mammals, and occasionally small hoofstock.

Mechanical Restraint Mechanical restraints (e.g., horse stanchions or cattle chutes) are typically associated with domestic hoofstock. However, similar mechanisms can be employed for the treatment of non-domestic species (Haigh, 1999). An example includes teaching a giraffe or rhinoceros to walk through and stand in a chute for daily physical exams and routine treatments (Figure 4.3).



Figure 4.1. Behavioral restraint of an Asian elephant allowing radiographs to be taken of the foot without sedation.



Figure 4.2. Manual restraint of a wild gopher tortoise.

It is also common for squeeze cages to be used for large carnivores and some primate species. Once mechanically restrained the animals can be induced with injectable agents or forced to breathe inhalant anesthetics. One of the main limitations of this method of restraint is that the animals must voluntarily enter, and they soon learn that the restraint device is where unpleasant procedures occur, which may limit future cooperation. Additionally, animals that actively resist the mechanical restraint become excessively agitated and can cause significant injuries to themselves or their



Figure 4.3. Mechanical restraint of a giraffe using a chute.

handlers. For example, broken canines are a relatively common adverse outcome associated with the use of squeeze cages in large felids.

Manual Drug Delivery Routes for Cooperative Animals

Oral The use of oral anesthetics is occasionally useful in zoological medicine. Some induction agents can be simply sprayed into the oral cavity or placed inside a food item that is then offered to the animal. Oral administration of various anesthetics has been accomplished using pineapple juice, maple syrup, peanut butter, marshmallows, and honey (Thurmon, Tranquilli, and Benson, 1996; Kearns, Swenson, and Ramsey, 2000; Mortenson and Bechert, 2001; Pollock and Ramsay, 2003). Carfentanil was administered to chimpanzees, tapirs, and bears trans-mucosally by mixing the injectable formulation of the drug into food. The transmucosal formulation of fentanyl was evaluated for use as part of a pre-anesthetic protocol in great apes (Hunter et al., 2004). Wild animals can be baited with medicated food that is placed in traps or spread out on the ground. One example is the use of oral alpha-chloralose to capture birds (Loibl et al., 1988; Hayes et al., 2003). In situations in which animals aggressively open their mouths when provoked, injectable anesthetics can be sprayed into the mouth or the nose for mucosal absorption (Grove and Ramsay, 2000). In practice, all of these methods of oral administration are difficult to apply consistently, as they require some measure of voluntary cooperation. Also, because the drug needs to be absorbed through the oral or nasal mucosa, it must remain in

contact with the mucosa and not swallowed. Generally, the inductions are prolonged and often unpredictable, but may occasionally work as pre-induction sedation.

Hand-Held Injection Hand injection is the most direct method of administering induction agents to an animal. It usually requires either exceptionally cooperative behavior or restraint for proper placement. For an effective intramuscular injection, even a restrained animal must be approached quietly and given the injection quickly.

The process of administering a hand injection generally involves the following steps:

- 1. A plastic disposable syringe with Luer-lock hub is selected to avoid needle detachment.
- 2. A large-gauge needle is selected to prevent breaking the needle during injection and allow fast deposition of the drug.
- 3. The filled syringe is then grasped between the index and the middle finger with the thumb over the plunger.
- 4. A proper injection technique requires a quick flick of the wrist so that the plunger is pressed as the needle begins to penetrate the skin.

Slower placement of the drug, with aspiration prior to injection, will rarely succeed in unrestrained non-domestic species. The hand injection method of drug administration is considered dangerous for the person injecting the anesthetic. Trauma from bite wounds, kicks, and crushing injuries are common. Of equal concern is the possibility for self-injection subsequent to the animal's sudden movements or exposure to aerosol sprays from a broken syringe. Therefore, hand administration of potent narcotics such as carfentanil is not recommended.

Pole Syringes A Pole syringe is essentially a hand injection with the added safety of a long pole. They were primarily developed for use in chute, cage, or traprestrained animals. This allows the operator to avoid some of the potential trauma associated with direct hand injections. However, this added safety is at the expense of control of the injection process. Poorly restrained animals invariably react to the needle by moving away or attacking prior to full injection. Similar to the hand injection, the technique requires a quick delivery through a large gauge needle (14 to 18 g). The needle is inserted in a large muscle, and then the pole is held in position until the drug is deposited.

There are three types of pole syringes. The pressure pole syringe is a typical syringe body with an extended plunger to provide extra length. Once inserted, the plunger is pushed against the resistance of the animal's body. In the second type, the extension pole is attached to the body of the syringe with a second internal

extension that is manually depressed to deposit the drug. The final type has a mechanism that has a spring or pressurized gas loaded plunger that is triggered when the needle presses on the skin. Although considered safer than hand injection, animals may still react to the needle and cause injury by moving or misdirecting the pole syringe.

REMOTE DELIVERY SYSTEMS FOR UNCOOPERATIVE ANIMALS

Unfortunately, in zoological medicine, many anesthetic procedures are performed on uncooperative animals for a variety of reasons. Animals that are not acclimated to human contact generally become agitated and aggressive when approached. This occurs in free-living species or many captive animals when routine direct human contact is discouraged. Some species, such as large carnivores or hoofstock, pose significant inherent risks to the veterinarians and keepers that preclude the possibility of using behavioral or physical restraint. Finally, even in cooperative or human-habituated animals, trained behavior can significantly change because of illness or pain so that the training no longer helps facilitate direct anesthetic drug delivery methods (Figure 4.4).

When injectable anesthetic agents are used in unrestrained non-domestic species, a remote delivery system consisting of a dart and projector is often the most practical option. Darts can be projected via a blowpipe, compressed air gun, or powder cap-charged gun are discussed later (Bush, 1992). All darts have four basic components: a drug storage compartment, a method of injecting the drug, a needle to penetrate the skin, and a stabilizer for accurate flight. The commercially available darts differ in their methods of drug expulsion, materials used in their construction, drug payload volume, and dart attachments such as the needle or tail. For this chapter, the method of drug delivery will be used to distinguish the darting systems.



Figure 4.4. Use of a blowpipe for short-range injection of an Indian rhinoceros that would react if hand injected.

Several home-made dart and projector systems have been described in previous literature (Haigh and Hopf, 1976; Warren et al., 1979; Barnard and Dobs, 1980; Lochmiller and Grant, 1983). This description and discussion of equipment is limited to those drug delivery systems that are commercially available. The choice of delivery systems is subject to the clinician's preferences, needs, or experience, but most commercial systems can be very effective when used by experienced operators. The similarity between available equipment systems allows some interchange of components that can be configured to meet the clinician's specific preferences. However, this interchangeability can also make using these products confusing when mixed together, and may lead to dart failure caused by subtle differences in the darting systems. Generally it is recommended that one system be purchased, as the manufacturers have developed product lines that are effective and reliable when used as designed.

Historical Development of Remote Delivery Systems

The remote delivery of drugs was first used by indigenous hunters with poison-tipped projectiles (Bush, 1992; Nielsen, 1999). Plant extracts containing curare were used by pre-Columbian South American Indians to produce effective neuromuscular blockage and muscle paralysis in animals. When these poison-tipped darts are projected with long blowpipes they can be delivered by experienced hunters with extraordinary precision and lethal effect. As the purpose of these hunters was to kill, the precision dosage delivery and margin of safety were not important considerations.

Until the second half of the twentieth century zoological collections relied on manual restraint as the primary means of administering veterinary care. These restraints were dangerous for both the humans and animals, often resulting in stress, injury, and occasional animal mortalities. In the mid 1950s a remote delivery device was described in the literature (Hall et al., 1953). It consisted of a metal drill bit with a gallamine and glucose paste packed into the groves. The bit was attached to a dart and delivered with a Crossman air gun. Once the animal was paralyzed and the procedure completed, the gallamine was reversed. Although effective, the paste was absorbed slowly; therefore, a flying syringe was developed to deliver liquid injections (Crockford et al., 1958). This aluminum dart used an acid-base reaction to inject the drug. After extensive modifications and improvements to this dart, it became the prototype for many of the modern darts in use today (Bush, 1992). Subsequently, plastic two-chambered gas darts were introduced to zoological medicine and developed into several commercial darting systems (Bush, 1992). For further details, several authors have reviewed the development of darting equipment over the past 40 years

(Harthoorn, 1976; Fritsch, 1982; Bush, 1992; Fowler, 1995; Nielsen, 1999).

Dart Types

Two-Chambered Compressed Gas Darts These darts are lightweight, two-chambered, and usually made of plastic or occasionally aluminum. The dart body is divided into dual chambers by a movable, rubber syringe plunger in the center (Figure 4.5).

The anterior drug chamber is bounded by the central plunger and a syringe hub that accepts a needle at the front of the dart. The posterior gas chamber is bordered anteriorally by the central plunger and a second, smaller movable plastic plunger in the back of the dart. The posterior plunger acts as a one-way valve that allows gas to be inserted through the posterior hub, but then occludes the posterior hub to prevent gas escape. The caudal part of the dart body has a syringe hub that accepts a tailpiece. The dart needles are hollow with a sharp, sealed tip. Several millimeters from the tip, the needles have an opening cut into the side for the medication to come through. A small silicone sleeve covers this opening (Figure 4.6).

These darts are charged by placing the drug into the anterior chamber and compressed gas into the back chamber. The pressurized gas may be air introduced manually with an adapter attached to a syringe or butane liquid placed into the posterior chamber of the dart (Figure 4.7).

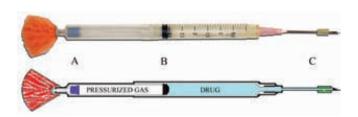


Figure 4.5. Photograph and illustration of a two-chambered compressed gas dart. **A.** Posterior plunger that is a one-way valve allowing compressed gas to be introduced, but preventing escape. **B.** Movable central syringe plunger that divides the two-chambers of the dart. **C.** Side ported needle with a silicone sleeve occluding the port.



Figure 4.6. Photograph of two-sided ported needles. **A.** This needle has the side port exposed. **B.** A similar needle with a silicone sleeve occluding the port.

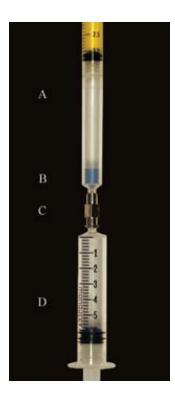


Figure 4.7. Photograph of a two-chambered compressed gas dart being filled. **A.** Posterior chamber of the dart. **B.** Posterior plunger that is a one-way valve allowing compressed gas to be introduced, but preventing escape. **C.** Coupler that is needed to allow air to pass from the syringe to the dart. **D.** Standard syringe used to force air into the dart.

Leakage of fluid is prevented by the silicone sleeve occluding the needle vent. As the needle enters the skin, the sleeve remains on the skin surface exposing the needle vent. The pressurized gas then pushes the central plunger forward and forces the drug out of the anterior chamber and through the needle. If the darts and needles are cleaned and maintained between usages they are reusable. The plastic darts can be gas sterilized and the needles can be autoclaved or gas sterilized.

Because this dart type is relatively lightweight and there is slow deposition of drug over several seconds, the injection is non-traumatic to the animal. The dart's sharp needles make them ideal for penetration of most skin types. With proper selection of needle lengths and dart sizes these darts can be used safely on a large variety of species. They are generally used for short ranges and preferably during good weather conditions, as their trajectories are easily affected by wind gusts. The primary disadvantages are that they can be destroyed by hitting unintended solid objects and their complexity makes them prone to dart failures.

Loading a two-chambered plastic dart involves the following steps:

- 1. An appropriate sized sterilized dart is removed from the package.
- 2. The dart is inspected for cracks and abnormal shape.

- 3. The dart is then tested by placing air pressure in both compartments to make sure that the plungers move correctly and the dart does not leak. A metal connector is needed to couple regular 6- or 12-cc syringes to the hub of the dart and inject air into the posterior chamber.
- 4. Next an appropriate sized, sterile, needle is selected. It must also be inspected for patency and to make sure that it does not have a burr at the tip or is bent from a previous impact.
- 5. The needle is then lubricated with sterile ointment and a silicone sleeve is placed over the needle tip and slid down over the needle vent. The sleeve is moved up and down the needle several times to be sure it moves easily before it is placed over the vent opening in the needle.
- 6. The needle is placed onto a syringe and air is forced into the needle to confirm that the sleeve has occluded the needle vent.
- 7. The dart is loaded by first displacing the posterior plunger (one-way valve) with a venting pin to make sure the posterior chamber is not pressurized.
- 8. The central plunger is then positioned to provide the correct volume for the drug in the anterior chamber.
- 9. The needle of a second syringe containing the drug is inserted through the anterior hub and the anterior chamber is then filled with the drug.
- 10. The needle with the pre-placed silicone sleeve is attached to the dart.
- 11. A safety cap is placed over the end of the needle until the dart is ready to be charged.
- 12. The dart is held in a vertical position with the needle pointing upward.
- 13. The dart is charged with either air or butane placed into the posterior chamber. The air or gas is forced in through the posterior hub, around the one-way valve, and into the posterior chamber of the dart. When properly charged, the rubber plunger at the back of the dart will be firmly pressed against the caudal portion of the posterior chamber.
- 14. The tailpiece is attached to the posterior hub, making the dart ready for use.

Blow Darts There are several types of two-chambered darts that use compressed gas to push the drug into the animal (Figure 4.8).

The first is the blow dart, which is constructed of lightweight clear medical-grade plastic used in disposable plastic syringes. The blow dart body usually has a Luer-lock syringe tip hub on the anterior drug compartment. The needle of the blow dart is sharp, constructed from a modified hypodermic needle that has a tip that is soldered closed and an opening cut into the side (Figure 4.9).



Figure 4.8. Photograph showing the difference between two types of two-chambered compressed gas darts. A. Blow dart. B. Molded nylon dart.



Figure 4.9. Photograph of two needle types used in two types of two-chambered compressed gas darts. **A.** A hypodermic needle that has the sharp tip occluded with solder used in blow darts. **B.** A thicker, blunter, machined needle used in molded nylon darts.

Because of blow darts' light weight and sharper needles, they are meant to be projected by blowpipes. They are most accurate when used indoors. Blow darts should never be used in ${\rm CO}_2$ or powder propelled projectors as their light construction causes erratic flight at high velocities and they often shatter on impact.

Molded Nylon, Two-Chambered Plastic Darts These darts are heavier than blow darts and constructed of opaque synthetic polymer plastic (molded nylon). The construction of the dart body is more robust and often reinforced. The anterior hub has a thick collar to better seat the needle and provide additional strength to the needle attachment. These needles are machined from a thicker metal that resists bending or breaking better than the modified hypodermic blow dart needles.

These heavier darts are designed for use in CO_2 or compressed air powered projectors. They have improved ballistic properties that allow them to fly true at higher velocities. They are also made to withstand greater impact forces. This gives these darts a much greater range and ability to be used outdoors in moderately windy conditions. The blunter needles have no difficulties penetrating most animal skin when powered by these projectors; however, they are ineffective when projected with a blowpipe. When used correctly and at

appropriate distances these darts are safe and cause only minor trauma. A variety of needle sizes are available. They can be fitted with barbs to decrease bouncing out of the animal. Impact absorbers also can be placed at the base of the needles to prevent them from penetrating beyond the intended depth and decreasing dart trauma (Wiesner, 1998). The potential problems associated with these darts are that they can cause significant trauma when used with gas-powered projectors at inappropriate close ranges. Clinical experience has demonstrated that these darts can be embedded into the soft tissues of animals and cause long bone fractures.

Powder Explosive Powered Darts Explosive powered darts use a black powder explosive cap to generate the force needed to discharge the drug. A movable plastic plunger is placed into the center of the dart body to separate the drug from the explosive cap and trigger mechanism (Figure 4.10).

The anterior chamber holds the drug. The posterior chamber holds a metal explosive unit that contains an explosive cap, a weighted firing pin, and a spring that keeps the firing pin away from the cap (Figure 4.11).

The explosive unit is set behind the caudal aspect of the central plunger, and the back of the dart is sealed with a tailpiece. The needles are hollow, forward ported, and do not need to be capped. The needles come in a large variety of lengths and are usually barbed.

These darts are loaded with the drug by placing the drug into the anterior chamber. When the dart hits the skin of the animal the needle penetrates and the body of the dart is stopped by the skin surface. The forward momentum of the dart is carried to the metal firing capsule where the small spring is overpowered and the firing pin impacts the cap resulting in an explosion. The resulting expanding gas within the posterior chamber rapidly forces the plunger cranially and the drug out of the needle. The injection occurs within approximately 0.001 seconds and can cause considerable tissue trauma (Kreeger et al., 2002). Additionally, the explosive rate of the injection causes a rocket effect that propels the dart

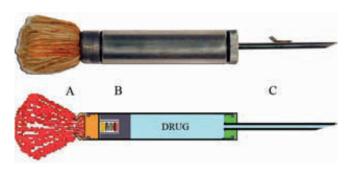


Figure 4.10. Photograph and illustration of a powder explosive powered dart. **A.** Yarn tailpiece that is threaded into the back of the dart body. **B.** Movable central syringe plunger that contains the explosive charge. **C.** Forward ported needle with a wire barb is threaded into the front of the dart body.

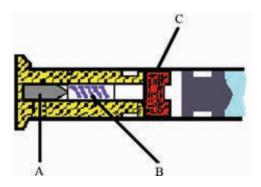


Figure 4.11. Illustration of the tail section and trigger mechanism of a Pneu-Dart powder explosive powered dart. **A.** Movable weight. **B.** Spring that holds the weight back. **C.** Explosive cap.

out of the animal. For the explosive unit to work the dart must strike the animal with enough force at a perpendicular angle to the target site to trigger an explosion. This necessary force can result in significant dart trauma in small or delicate species.

Modular Powder Explosive Powered Darts The Palmer Cap-Chur dart kit comes disassembled in components so the operator can assemble the dart configuration that is needed. The body is an aluminum 12.6-mm (50-caliber) tube with internally threaded ends. The aluminum syringe barrel comes in various lengths that can hold 0.5 to 20 ml of drug. The Palmer Cap-Chur charges come in three different powder strengths that are selected for the appropriate dart volume; yellow for 0.5 to 3 ml, orange for 4 to 10 ml, and red for 15 to 20 ml. Improper selection of the charge strength can lead to dart failure. The metal explosive charge fits with its closed, rounded, cranial end into a pocket in the caudal aspect of the central plunger (Figure 4.12).

The explosive unit must be oriented correctly with the open end facing caudally for the dart discharge. The back of the dart is sealed with a tailpiece that screws into the internally threaded dart body. The needle is

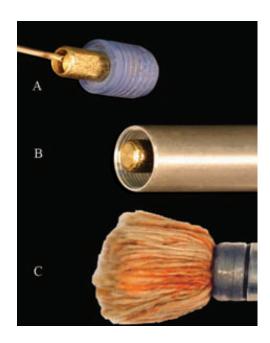


Figure 4.12. Photograph demonstrating the steps in assembling the tail section and trigger mechanism of a Palmer Cap-Chur powder explosive powered dart. **A.** The charge has been placed into the caudal pocket of the central plunger. The needle is pressing the weight and spring to demonstrate the proper orientation of the explosive charge. **B.** The plunger and explosive charge have been inserted into the posterior part of the dart body. **C.** The yarn tailpiece has been threaded into place.



Figure 4.13. Photograph of three needle types used in powder explosive powered darts. **A.** Pneu-Dart needle with a cone collar gel barb. **B.** Palmer Cap-Chur needle with small metal collar. **C.** Palmer Cap-Chur needle with wire barb.

threaded into the anterior end of the dart. The needles are hollow, forward ported, and do not need to be capped. The needles come in a large variety of lengths and with several barb styles (Figure 4.13).

This system is one of the oldest commercially available darts and has had many years of proven reliability. The variability in needle length and payload volume

(tube size) makes this the most versatile darting system. From one kit, darts can be configured with short needles for carnivores or very large needles and barrels used for elephants and rhinoceroses. The dart components, except the explosive units, are reusable if cleaned and maintained properly. Keeping the dart components sterile is challenging, but using unsterilized equipment may lead to dart-induced infections (Bush and Gray, 1972). The biggest weakness of the system is that the heavy darts and the explosive discharge of drug lead to tissue damage.

Loading a Palmer Cap-Chur dart involves the following steps:

- 1. The appropriate-sized sterilized dart components are removed from their packages.
- 2. The dart parts are inspected for cracks and abnormal shape. The needle, body, and tail are preliminarily assembled to insure proper threading and then passed through the syringe barrel of the projector to ensure that the dart passes freely.
- 3. A sterile, central, rubber, plunger is selected and then lubricated. It is placed inside the body of the dart, and the plunger is moved back and forth within the length of the body to ensure that it moves easily.
- 4. The plunger is positioned in the caudal part of the dart body.
- 5. An appropriate strength metal explosive unit is fitted into the pocket in the caudal aspect of the plunger. It is crucial to make sure that the explosive unit is oriented correctly, with the movable weight exposed caudally.
- 6. A tailpiece is selected and threaded into the caudal part of the dart body.
- 7. Next, an appropriate-sized needle with an acceptable barb style is selected. It must be inspected for patency and to make sure that it does not have a burr at the tip or is bent from a previous impact.
- 8. The needle is then threaded onto the cranial part of the dart body.
- 9. The dart is loaded by passing the needle of a syringe containing the drug through the dart needle lumen and depositing the drug into the anterior chamber of the dart.
- 10. Sterile water is used to completely fill the remaining volume in the anterior chamber of the dart.

Prefabricated Powder Explosive Powered Darts Prefabricated versions of the powder explosive powered darts are commercially available. The explosive system is similar, except that the explosive mechanism is preplaced in the dart by the manufacturers. The dart is made of a combination of aluminum body and needle and a plastic tailpiece. The dart is purchased as a complete unit and cannot be taken apart. The function and limitations are similar to the modular systems.

The simplicity of the pre-purchased dart makes this an appealing product. The operator selects the dart volume, needle length, and barb configuration that will be needed for the anesthetic event. Most needles come with a green gelatin collar or barb to prevent the darts from being ejected from the skin when the dart discharges. Loading the dart is a simple matter of placing the drug through the dart needle and into the anterior chamber.

Pneu-Darts come in two types: the first is the "P" dart line, with a yellow tail, that is designed for blowpipes or CO₂ powered projectors. The other dart line is the "C" dart, with orange tailpieces, that are designed for the 22 blank powered rifles. The major differences are the diameter of the tailpieces are larger in the "C" dart to help engage the rifled barrel and the tensile strength of the spring in the explosive unit is weaker in the "P" dart.

Miscellaneous Dart Types

Aluminum Two-Chambered Compressed Gas Dart Palmer Cap-Chur produces a two-chambered compressed gas version of the explosive powdered dart line. This dart uses the threaded aluminum tube, but the standard explosive charge is replaced with a one-way valve system in the posterior chamber. There is also a closed needle with a side port vent and sleeve. This dart functions similarly to the two-chambered gas darts.

Chemical Powered Darts Chemical darts use an effervescent acid-base reaction to produce gas and thus inject the anesthetic (Figure 4.14).

The design has a two-chamber configuration with the chemicals placed in the posterior chamber. Prior to discharge the chemicals are kept apart. Upon impact, a variety of mechanisms have been devised to allow the chemicals to mix and produce gas (Bush, 1992). There are no chemical darts commercially available in the United States, but they are used and available in Africa and Europe (Nielsen, 1999). Because the drug compartment is not under pressure, open-ended needles can be used. The advantage is that the darts are easy to load and

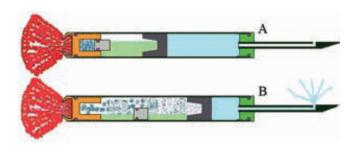


Figure 4.14. Illustration of a chemical reaction powered dart. **A.** The loaded dart prior to impact. The chemical reagents are kept separated by a weight occluding the chemical chambers. **B.** The dart after impacting the target and during discharge of the drug. The weight was dislodged and the chemicals have mixed and produced a gas that pushes the central plunger forward.

reliable in most field situations. The injection speed is slower than compressed gas or explosive charged darts, but this slow discharge is usually acceptable. The slow discharge is beneficial in that it causes minimal injection trauma and limited blow back from the dart.

Spring Powered Darts Spring powered darts are not currently commercially available in the United States. The design is similar to the two-chambered dart, except the posterior chamber is replaced with a spring to provide the injection force. The spring is attached anteriorally to the central plunger and posteriorally to the back of the dart body. Trigger mechanisms usually involved silicone capped needles that function similarly to the two-chambered darts. The dart body can be constructed of plastic or metal depending on the projector that will be used. The major problem with these darts is that the process of loading the dart was difficult and dangerous because of inadvertent spraying of the drug during the loading process.

Solid Drug Darts Solid drug projectiles can be used potentially to deliver anesthetics or sedatives. The principle of these solid bullets is similar to the original gallimine paste projectiles described from the 1950s. Several attempts have been made to develop a solid, lightweight, absorbable bullet (Bush, 1992). The current versions are made of various materials such as hydroxypropylcellulose that dissolve and absorb into the muscle of the animal (Jessup, 1993; van de Wijdeven, 2002). An example is the BallistiVet system that was developed for vaccination of domestic livestock, but can be applied to both captive and wild non-domestic species. As in the original descriptions of solid drug injection systems, the limitations of payload size and slow absorption are persistent obstacles in their use for primary induction of anesthesia.

Remote Delivery Projectors Compressed Gas Projectors

Blowpipes Blowpipes consist of a long lightweight tube with a mouthpiece on one end. A blow dart is placed in the end of the pipe and compressed gas is provided by the operator blowing with a rapid, strong breath through the tube. The longer the pipe is the greater the accuracy of the dart. Commercial blowpipes are available from several manufacturers in various pipe lengths, diameters, and shapes of mouthpieces. Selection is based on personal preferences for the mouthpiece and the diameter of the dart type selected.

Usage of a blowpipe requires practice. The pipe is held horizontally, and grasped in the hand opposite to your dominant eye. Look at the tip of the pipe and aim it onto your target. Inhale deeply and then rapidly exhale in a manner that approximates a combination of coughing and spitting through the pipe. Because of the slow dart velocity, the dart will tend to fly in an exaggerated

downward arc instead of a straight line. Effective blowpipe range is about 0.5 to 10 meters.

Blowpipes are by far the most versatile, inexpensive, silent, lightweight projectors available. In short ranges an experienced darter can have exceptional accuracy. The light darts combined with the slow velocity of the dart produce minimal impact and tissue trauma. The operator can adjust the dart speed instantly and therefore deliver the dart as gently as needed. Because darts occasionally leak and the mouth must be placed on the mouthpiece, it is not recommended to project darts with dangerous drugs such as concentrated narcotics using a blowpipe.

Blowgun Projectors A modification to the blowpipe is to add an external source of compressed gas to eliminate the need for the operator to exhale through the pipe (Figure 4.15).

These are designed to shoot the heavier machined two-chambered plastic dart or the type "P" Pneu-Darts. The basic components needed are source of compressed gas, control of the gas pressure with a combination of a pressure gauge and valve system, and a trigger mechanism. These systems can be powered either by air via a foot pump or by compressed carbon dioxide from a portable bottle. Pressure gauges and release valves allow the pressures to be increased or decreased as needed during darting. A detachable, long barrel is then mounted on either a pistol handle or a rifle stock. The rifles can be equipped with a telescopic sight. Typically, these projectors have barrels that can be interchanged to accommodate both 11- and 13-mm darts. The pistol is used for short range or indoors where space is limited. The rifles have more accuracy and are used outdoors. Careful selection of the dart type is important, as lightweight plastic blow darts will not fly correctly in these CO₂ powered projectors.



Figure 4.15. Photograph of two Dan-Inject blowgun type projectors. **A.** A model CO_2 PI pistol with an 11-mm barrel. The pistol is powered with a compressed CO_2 cartridge. **B.** A JM Special rifle with an 11-mm barrel. It is also powered by a compressed CO_2 cartridge.

These systems are quiet, reasonably accurate, and a simple means of darting exotics for distances up to 5 to 30 meters. Many veterinarians in zoological collections use this system exclusively.

Air and CO₂ Rifles and Pistols The next group of compressed gas projectors are the pistols and rifles with a barrel permanently mounted onto a triggered compressed gas power source (Figure 4.16).

The compressed gas power source can be provided by CO_2 bottles or an attached air pump similar to a pellet gun. These projectors generally lack accurate pressure gauges and valve systems with the ability to change the gas pressure. Instead, they often have two or three preset steps for selecting power levels. They are usually designed for 12.5-mm metal darts such as Palmer CapChur and type "P" Pneu-darts. Because of their short barrels, the pistols are notoriously inaccurate at long range. In contrast, the rifles can be very accurate at moderate distances. Both systems, when used at short range, can cause significant trauma because of the lack of accurate pressure control.

Powder Load Powered Rifles These rifles have permanently mounted barrels on a rifle stock. They are powered by 22-caliber blanks that come in several charge strengths with different amounts of powder. In the Palmer Cap-Chur system, brown is the weakest, followed by green, yellow, and red (Figure 4.17).

Although they lack pressure gauges, they often have methods of selecting power levels. These rifles are too powerful for short range or indoor use, but have good accuracy when used outdoors. These rifles have the longest effective range and can be used in windy conditions. They have 12.7 mm (50 caliber) and are designed for 12.5-mm metal darts such as Palmer Cap-Chur or type "C" Pneu-Darts.

Miscellaneous Projector Types

Crossbows and Bows Commercially available darts can be mounted on arrow shafts delivered with crossbow and conventional bows. In Africa, several Ju/'Hoan bushmen were given arrows with Pneu Darts attached at the tips. Using these arrows and their archery hunting techniques they were successfully able to immobilize free ranging lion and leopards (Stander et al., 1996). Archery based projectors are accurate, but if not controlled, the velocity of the heavy arrows will cause trauma to the animals.

Injection Collars Remote Injection collars can be placed on an animal prior to release and used to inject the animal at a later time (Jessup, 1993). Commercially available products have been used in white-tailed deer and wolves. The injection is triggered by remote control. Combined with telemetry and a safety collar release if the batteries are low, this can potentially be a valuable



Figure 4.16. Photographs of three compressed gas powered 12.7-mm (50-caliber) projectors. **A.** Palmer Cap-Chur Model #1300 mid-range pistol powered with two compressed CO₂ cartridges. **B.** Pneu-Dart Model 178B air pump rifle. **C.** Palmer Cap-Chur Model #1200 long-range rifle powered with two compressed CO₂ cartridges.



Figure 4.17. Photographs of two powder load powered 12.7-mm (50-caliber) projectors. These guns are very powerful and used only outdoors for long-range targets. A. Palmer Cap-Chur Model #1000 extra long-range rifle. **B.** Pneu-Dart Model 196 rifle.

tool for wildlife. Application of these collars in zoological collections has been limited, but may be practical in situations that require multiple immobilizations in animals that are difficult to dart.

Darting Accessories

Many manufacturers provide practice darts and targets for their equipment. Usage of these darts is cheaper than using operational darts and they are consistently weighted to help improve accuracy. Through practice the operator develops proficiency with the equipment and reliable accuracy. During this practice it is important to develop an understanding of the proper impact velocity that is needed to prevent excessive trauma.

Laser range finders and binoculars are useful in outdoor darting procedures. Calibrating the projector for selected distances is the best method of consistently producing accurate and atraumatic shots. Once the calibration is completed during practice sessions, using the range finder significantly improves range estimates and allows the operator to make confident and accurate projector settings. The binoculars are useful for selecting the target and then confirming that the dart has hit the animal. Darts that are buried in vegetation can be very difficult to locate. Some manufacturers offer darts that are equipped with radio locators. These can be very useful when dart recovery is mandatory, or tracking a darted animal is necessary.

Drug Delivery Problems

Dart Failure Although darts and their projectors have become indispensable tools in zoological medicine, darting problems are common. The most important factor causing a dart to miss the target is operator error from inexperience with the darting system. Accuracy and consistency are only developed with persistent practice. Each darting system has individual characteristics that must be learned by the operator.

Unfortunately all darting systems are prone to high failure rates, and even when the darts hit their intended target, many fail to discharge. As the complexity of the darts increases, this becomes the most important factor leading to dart failure. Careful preparation and testing of the darts is an essential step prior to each darting. The various darting systems each have their critical or failure prone components that must be checked by the operator. Maintaining the equipment in portable organized kits helps insure that the proper components are available and facilitates the darting procedures (Figure 4.18).

Examples of common problems are explosive charges that fail to fire, blocked dart needles, and central plungers that stick. Ambient temperatures can affect dart function and the performance of compressed gas darts. In very cold temperatures darts may fracture on impact, drugs can freeze or become thick, and compressed gas exerts less pressure, causing incomplete discharges.

Drug Failure The selection of anesthetic drugs is beyond the scope of this chapter, but can definitely cause immobilization failures. Improper deposition of the darted drugs can also produce unexpected results.



Figure 4.18. Photograph of a darting kit with essential components separated into compartments. Note that a radio is included to provide emergency communications.

Darts that deposit drugs into vascular structures or medullary cavities of bones can have rapid onset similar to intravenous administration. Conversely deposition into skin, subcutaneous space, tendons, or other poorly vascularized tissues can have slow absorption. Some clinicians recommend the usage of hyluronidase to improve absorption of drugs injected with darts (Kock, 1992).

Drug interactions when mixed into a syringe must be considered, but have been poorly studied. Environmental conditions such as freezing or heating may also alter drug potency. Storage of drugs in pre-loaded darts is questionable, as the drugs' potency and purity may change with time (Kreeger, 2002).

Aerodynamics of Darts Darts have poor ballistic properties when compared with bullets or arrows. With variable shapes and shifting liquids they are often very erratic in flight. As an example, bent darts or needles damaged by previous impacts can radically alter the flight trajectory. Aside from the shape, the velocity of the dart as it exits the projector is an important variable in prediction of the dart's trajectory. Fast muzzle velocities produce flat flight trajectories similar to a bullet. Although accurate, these faster velocities are associated with severe impact trauma and dart malfunctions. Further, all darts, even when properly loaded and balanced, will destabilize at very high velocities. This forces all darting systems to use relatively slow muzzle velocities. At these slower velocities the darts tend to form a downward arced trajectory that is increased as the darting distance increases. This arc must be anticipated and an experienced darter will compensate appropriately.

The tailpiece is designed to provide the dart with aerodynamic stability (Figure 4.19).

Available tails range from finned tails similar to archery arrows that are considered the best, to cloth tail stabilizers that can cause problems if they are asymmetrical. Rifling of the projector barrel is a method of increasing flight stability by forcing the projectile to spin on its horizontal axis (Figure 4.20).

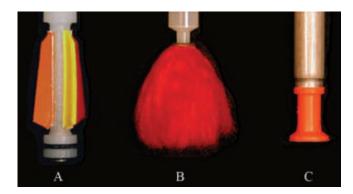


Figure 4.19. Photograph of three types of dart tails. **A.** Four fin tail from a Dist-Inject mini-ject easy dart. **B.** Cloth tail from a Dan-inject molded S series dart. **C.** Plastic tail from a Pnue-Dart C dart.



Figure 4.20. Photograph through the barrel of a rifle barrel showing the spiral rifling needed to cause a dart to spin on its horizontal axis during flight.

Unfortunately, few darts are capable of engaging the rifled barrel surface and therefore do not spin in flight. Additionally, some dart tails, such as cloth and finned configurations, actually resist the horizontal spin that the rifled barrel is intended to provide.

In addition to the aerodynamic considerations of unobstructed flight, environmental conditions associated with outdoor darting can have significant effects on dart trajectories. Winds and wind gusts can cause darts to fly in unexpected directions. Helicopter down drafts can also affect darts. Because of their light weight, plastic darts are particularly prone to this problem. Objects such as plants may deflect the dart.

Animal Injury Severe tissue injury, including hemorrhage, necrosis, and bone fractures, can occur whenever darts are used. Any projectile with a needle can cause an injury when it hits an animal in an unexpected location. Sudden movements from the targeted animal can lead to inadvertent injury to either the target or other animals in the group. Examples of dart injuries to the eye, thorax, abdomen, and testicles are common. It is ultimately the operator's responsibility to only take shots that are likely to hit the expected target.

The site selection for darting is important. In most animals the muscles of the upper hind legs are the safest selection. Occasionally the base of the neck or the triceps can be targeted. When selecting the site, the animal must have sufficient muscle mass to allow for injection of the drug and safe impact of the dart. Most darting systems have a variety of needle selections that must be chosen to limit tissue trauma while effectively providing penetration and injection of the drug into the

muscle. Needle length is selected on the thickness of the animal's skin and the expected depth of the muscle mass. Inappropriately long needles have the potential to fracture bones on impact. Thickness of the needle is dependent on the potential for the needle to break on impact and broken dart needles retained in muscle tissue have been reported (Cohn, 1998). Darts primarily cause trauma on impacting the animal in direct relationship to the kinetic energy of the dart (Karlsson and Stahling, 2000; Kreeger, 2002). This energy can be estimated by knowing the mass and speed of the dart in the following relationship:

$$KE = 1/2 \text{ (Mass)} \times \text{(Velocity)}^2$$

It is important to note that the velocity is squared and therefore has the greatest influence on the injuries caused on impact. Thus, heavy darts are not always more harmful for the animal (Kreeger, 2002). All darts require enough kinetic energy for the needle to enter the skin and trigger discharge, but excessive amounts are associated with trauma and dart failure. In extreme situations the whole dart can be imbedded into the muscle or fracture a bone.

Darts can also injure tissues by forceful injection of drug. This is particularly true of large-bore, open-ended needles that are discharged with explosive force. Evidence of tissue injury and necrosis has been documented with these types of darts (Wiesner, 1998).

Needle trauma caused by movement of the needle after discharge can be significant. Often the first reaction of a darted animal is to jump, run, or remove the dart. Barbs and collars on many dart needles are designed to keep the darts in the animals, but if they are retained for long periods or forcefully removed they can lead to injury.

Infection of the dart site is generally rare, but can cause serious complications to routine darting procedures. The needle of the dart enters unprepared and often grossly contaminated skin. Unsterile darts and drugs can further inoculate the injection site. Once bacteria are introduced they grow well in the traumatized tissues associated with the dart site. This combination of trauma, large needles, and unprepared injection site can produce significant and deep wounds that are likely to develop into clinical infections. Many practitioners recommend the use of prophylactic antibiotics and local wound care for every dart site. Most darting systems can be sterilized prior to use and aseptic techniques can be used during the dart preparation (Bush and Gray, 1972).

Human Safety Concerns during Darting Procedures

Darting systems should be considered firearms and treated with the same precautions of basic gun safety to prevent accidental discharges. As in animals, the ballistic properties of all darts are able to inflict serious injuries to people. Darts are subject to radical changes in

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Manufacturer and Dart Description	Dart Type	Payload Volume (ml)	Dart Diameter (mm)	Needle Sizes (mm)	Tailpieces	Recommended Projector
Dan-Inject blow dart syringe Telinject blow dart syringe	Two-chamber Two-chamber	1.5, 3 1, 2	11.8 9.5	$1.1 \times 25 \text{ or } 1.2 \times 38$ $0.9 \times 25 \text{ to } 1.2 \times 38$	Orange cloth Yellow cloth	12-mm Dan-inject 1.23 or 1.8-m (2-piece) blowpipe 10-mm Telinject 1- or 2-m blowpipe
Telinject blow dart syringe	Two-chamber	1, 2, 3	10.8	(3 gauges and 4 lengths) $0.9 \times 25 \text{ to } 1.2 \times 38$ (3 gauges and 4 lengths)	Orange cloth	11-mm Telinject 1- or 2-m blowpipe
Telinject blow dart syringe	Two-chamber	5	14.0	0.9×25 to 1.2×38 (3 gauges and 4 lengths)	Red with yellow cloth or plastic	15-mm Telinject 1.5 blowpipe
Dist-Inject mini-ject "softy" blow dart svringe	Two-chamber	3.8	10.8	1.1×25 or 1.2×35	Red cloth	11-mm mini-ject 0.9-m blowpipe
Maxi-Ject veterinary	Two-chamber	1,2	6.7	1.9×25 or 1.2×28	Yellow cloth	10-mm maxi-ject 2-piece 1-m blowpipe
Maxi-Ject veterinary	Two-chamber	3	10.7	1.9×25 or 1.2×38	Red cloth	11-mm maxi-ject 2-piece 1-m blowpipe
Maxi-Ject veterinary	Two-chamber	5	13.7	1.2×38	Red with	14-mm maxi-ject 2-piece 1-m blowpipe
syringe dart Telinject "Vario"	Two- chamber	1,3	10.8	$1.5 \times 20 \text{ to } 2.0 \times 60$	yellow cloth Red cloth	11-mm Telinject Vario pistol or rifles
Telinject "Vario"	Two-chamber	5, 10, 15, 20	12.2	(2 gauges allu o lenguls) 1.5 × 20 to 2.0 × 60	Red with	13-mm Telinject Vario pistol or rifles
molded plastic syringe Dan-Inject "S" series	Two-chamber	1.5, 3	10.7	(2 gauges and 8 lengths) $1.5 \times 20 \text{ or } 2.0 \times 100$	yellow cloth Red cloth	11-mm Dan-inject model PI pistol or JM/IM
molded plastic syringe Dan-Inject "S" series	Two-chamber	5, 10	12	$1.5\times20\ \mathrm{or}\ 2.0\times100$	Red with	injection rifles 13-mm Dan-inject model PI pistol or JM/IM
molded plastic syringe Dist-Inject "mini-ject 2000"	Two-chamber	3,5	10.8	1.1×25 or 1.2×35	white cloth Red cloth	injection rifles 11-mm model 45 delta pneumatic 0.35 m
molded plastic syringe Dist-Inject mini-ject "easy" molded plastic syringe	Two-chamber	3,5	10.8	1.1×25 or 1.2×35	Orange and vellow fins	blowpipes, or model 70 rifle with 11 barrel insert 11-mm model 45 delta pneumatic 0.35-m blownines
Palmer Cap-Chur aluminum "Air inject" syringe	Two-chamber	1, 2, 3, 4, 5	12.5	2.5×19 to 2.5×38 (11 lengths) (side port with nose plug)	Tetra plastic tail	12.7 Palmer Cap-Chur short, mid, and long range CO_2 projectors
Dist-Inject mini-ject "unic" molded plastic svringe	Chemical	3.5	10.8	$1.1 \times 25 \text{ or } 1.2 \times 35$	Red cloth	11-mm barrel insert in model 70 or 50 rifles
Pneu-Dart "P" aluminum dart	Explosive	0.5,1	12.5	2.0×6 to 2.0×50 (7 lengths)	Yellow plastic	12.7-mm Blo-Jector blowpipe
Pneu-Dart "P" aluminum dart	Explosive	0.5, 1, 1.5, 2, 3, 4, 5, 6, 7, 8, 10	12.5	2.0×6 to 2.0×50 (7 lengths)	Yellow plastic	12.7-mm X-caliber gauged $CO_2/rifle$ $CO_2/rifle$ air model 178B air rifle, or various pistols
Pneu-Dart "C"	Explosive	0.5, 1, 1.5, 2, 3,	12.7	2.0×6 to 2.0×50	Orange plastic	12.7-mm model 193, 194, 196, and 2000
arummum dari Palmer Cap-Chur aluminum dart	Explosive	5, 7, 10, 15, 20 5, 7, 10, 15, 20	12.6	(7.1Eng_{113}) 2.5 × 13 to 2.5 × 76 (11 lengths)	Yarn or plastic "Tetra"	12.7-mm #1300 Mid range pistol, #1200 long-range CO_2 rifle

trajectory when they are deflected by wind, obstacles, and bouncing off animals. Therefore, it is imperative that the operator considers the position of all the personnel around and particularly behind the target before the trigger is pulled.

All the dart systems described in the preceding are designed to automatically discharge drugs, making them even more dangerous when they hit a human. In rare occasions, darts may expel the drug prior to full needle penetration or after bouncing out of the skin. In these cases the drug can be aerosolized or sprayed onto the surface of the animal and can be a source of drug exposure. Emergency plans to deal with accidental drug exposure need to be in place prior to the immobilization procedures. It is important to have effective emergency communication equipment such as a cellular telephone or two-way radios.

The most important safety considerations are proper planning and familiarization with the drug delivery method selected (Table 4.1). Having each procedure well planned is essential so that everyone is cognizant of their roles and safety considerations. Prior practice and familiarization with the equipment make the operator more confident and effective in delivery of the anesthetics. Ultimately the responsibility for the safety of an anesthetic delivery is on the anesthetists and the operator of the equipment.

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5

Mobile Inhalant Anesthesia Techniques

Bruce Heath

INTRODUCTION

Movable or portable anesthesia has been in use in MASH units and military or civil defense situations for many years. Field biologists needing more sophisticated testing and complete access to their field animals often require more time than that which can be provided with injectable anesthesia. This necessitated the invention or practical simplification of veterinary large and small animal gas anesthesia equipment and techniques to facilitate utility in field situations. Hospital and zoo mobility facilitates movement of patients to radiology or multiple surgical locations complete with monitoring equipment. More elaborate arrangements have to be made to do the same on remote Alaskan rock islands. Lightweight durable packaging for helicopter, surfboat, float plane, and backpack transport had to be devised. Scientific crews are now routinely investigating species including mice, weighing grams, up to marine mammals, at 600 kg. We are able to provide as much as 7 hours for elaborate surgery and sophisticated isotope studies in many quite remote locations worldwide, including arctic, Antarctic, land, and ocean situations. Patients commonly receiving inhalant anesthesia in the wild include a full range of species and weight sizes. Examples include elk, deer, antelope, black-footed ferrets, marine mammals, snakes, prairie dogs, rodents, and many other individual wild and zoo stock species (Table 5.1).

CAPTURE ISSUES AFFECTING ANESTHESIA

Simple mechanical capture has been shown to result in statistically more captures with fewer losses than drug capture (Spraker, 1993). Traps, snares, nooses, netting, and other SCUBA diver, air- or land-based mechanical mechanisms are safer than using drug delivery of multiple or massive doses, although they sound like rough treatment for a brief period of time. Mechanical capture should be used judiciously and carefully. Rest should be

allowed after capture so the animals can become acclimated to their new surroundings and recover to their pre-capture stress cortisol levels. Capture stress or myopathy is always a part of wildlife management, and is seen in a great scale of gradation, with a range of responses from mild to fatal experiences. Quiet box rest and hoods or masks give many of our patients great protection that are normally fight-flight psyche individuals.

Instability and difficulty with anesthetic management may be exaggerated if the animal is rushed from capture straight to anesthesia, so a period of rest before anesthesia is advised. Forty-five to sixty minutes are allowed after dive capture of Steller sea lion juveniles before anesthesia (Johnson, Gelatt, and Heath, 2004). This results in a greater level of stability in the anesthetic period than those that are rushed, especially in temperature management. If darting drugs are a part of patient capture, use volatile vapor anesthesia extremely sparingly (Heath, Calkins, and Spraker, 1996).

Isoflurane alone, given by mask, has resulted in very few losses. Records on over 5,000 sea lion pups, caught by hand and masked for various procedures in Alaska, Russia, California, and Oregon have resulted in fewer than seven deaths. Those have been shown by necropsy to be either related to mishaps in crowding while herding animals or caused by very poor health. Most were severely parasitized individuals with anemia with packed red cell volumes in the range of 10% to 12%.

Over 600 free-ranging juvenile sea lions captured by divers in Alaska have been brought to ship-based hospital shacks and safely anesthetized. Records show only four losses, and these resulted from operator or machine failure (Johnson, Gelatt, and Heath, 2004).

Pronghorn antelope in the Great Plains states are a species that is highly excitable and suffers high losses because of heat exhaustion. Simple mechanical capture with coral/fence nets coupled with hoods and masking results in fewer fatalities than drug administration (Fowler, 1993). Helicopter cannon netting of Colorado bighorn sheep and apple baiting of large groups have

Table 5.1. Known wildlife and zoo mobile units for inhalants.

Species	Agent(s)	Location	Project	Agency
Zalophus	Isoflurane	CA, OR, WA	Study	Nat Marine Mammal
				Lab Seattle
Eumetopias	Isoflurane	Alaska	Juveniles	Nat Marine Mam Lab Seattle &
			Adult cows and pups	Anchorage
Eumetopias	Iso Sevo	PWS, Aleutians, AK	Juveniles	AK F & G Anchorage
Phoca	Iso	Aleutians, SE AK	Adults and pups	AK F & G Juneau
Avian Sea birds	Iso	AK Russia	Population study	AK Sealife Ctr
Eumetopias	Iso	AK, Russia	Adult cows & pups	AK Sealife Ctr
Eumetopias	Iso	Vancouver, Canada	Pups cows	Vancouver Aquarium
Eumetopias	Iso	Kamchatka, Russia	Pups	Inst. of Geography
Fresh water seals	Iso	Black Sea, Russia	Adults	Univ Cal LA
Zalophus	Iso	Mystic, CT	Health Multiple	Mystic Aquarium
Zalophus, Phoca	Iso	Sausalito, CA	Multiple	Marine Mamm Center
Multiple	Iso	Calgary Canada	Multiple	Calgary Zoo
Multiple	Iso	Singapore	Multiple	Singapore Zoo
Zalophus	Iso	Santa Cruz, CA	Multiple	U Cal Santa Cruz
Black foot ferret	Iso	New Mexico	Reintroduction	Turner Endang Fund
Black foot ferret	Iso	WY, MT, SD, ND	Reintroduction	BLM & Div of Indian
Black foot ferret	Iso	WY, MT, UT, CO	Reintroduction	US Fish & Wildlife
		SD, ND, AZ	Endangered sp.	Multiple BLM units
Mule & white tail	Iso	Colo	CWD study	CSU Prion Path lab
Mule deer	Iso	COLO	CWD diagnosis	Colo Div Wildlife
Big horn sheep	Iso	COLO	Stress study	Colo Div Wildlife
Prairie dogs	Iso	COLO	Habitat	CSU Biology
Black bear	Iso	CO, WY	Hibernation	Wy St U Biology
Canine feline	Iso	Mexico, Guatemala	Spay & neuter	Vidas international
Canine feline	Iso Halo	Mexico	Spay & neuter	Priv Vet Practices
Skunks & badgers	Iso	Nebraska	Biology studies	Univ Nebraska
Rodents	Iso	North Carolina	Biology	Schiele Mus Nat Hist
Multiple sm mamm	Iso	Colorado	Access disease	CDC
Multiple sm mamm	Iso	Colorado	Access disease	Inhausen Resch Inst
Kit fox	Iso	So. Dakota	Biology	BLM
Multiple	Iso	Arizona	Multiple	Ariz Fish & Game
Multiple	Iso	CO, WY	Multiple	US Parks Scvs
Richardson's ground squirrel	Iso, Sevo	Saskatchewan	Disease surveys (serology)	Univ of Sask

resulted in minimal losses even though this species often suffers from lung worm infestations and fragile health of individuals.

The "normal" hospital or home experience with tranquilizing drugs given in calm settings to domestic animals does not apply to capture myopathy and heat stress in wild patients. Wild capture is actually the wrong time to give drugs (Fowler, 1993; Spraker, 1993). Avian species constitute a large group of research activity, and inhalent anesthetics are often the safest choice for avian anesthesia (Tuomi and Mulcahy, 2005).

Support research continues on endangered and migratory species in the arctic north, including multiple species in mobile situations. An implant bulletin board network may be valuable to many readers. Contact Dr. Mulcahy at daniel_mulcahy@usgs.gov.

INHALANT EQUIPMENT

Adequate equipment is easily obtained from many companies. Innovative persons can also make their own

units from pieces. Inhalant equipment in the full range from non-rebreathing to large animal size circuits is available. The objective in fieldwork is to devise the simplest and lightest weight units to perform the task. Once at your field destination it is always wise to fully inspect all pieces for breakage, thin line cracks, lose hoses, and unforeseen missing parts. Airlines, helicopters, and shipping agents seem to delight in bouncing packages around, even though labeled fragile and well packed.

Small patients from grams up to 10 kg can be anesthetized with non-rebreathing circuits. Baine circuit units come in various lengths, which lend convenience in fieldwork, allowing you to go to the patient in many awkward positions. Added vaporizer delivery tubing length is helpful also. Modified Jackson-Rees non-rebreathing units are less expensive, and supplied as disposable units. For very small species such as mice, rats, and ferrets, you can easily fashion masks from syringe cases. A very handy simple mask with a built-in exhaust tube is the familiar Simplex IV delivery set used for intravenous delivery in large animal practice. Inhalant

chambers can be fashioned from various-size plastic nut jars with screw-off lids. When working outdoors, scavenge is less of a problem, but if you move your equipment into camper shells, shelter enclosures, or laboratory settings, then attention should be paid to proper scavenge practices. Laboratory hoods suffice here if they lead to outdoor air circulation.

Specially insulated anesthesia units have been made for extreme cold climates by Gales et al. (in press).

Small animal circuits suitable for 10- to 15-kg patients include tabletop units such as supplied by Surgivet (Waukesha, WI) and Matrix (Orchard Park, NY).

Tripod units (Seven Seven Anesthesia, Ft Collins, CO) lend the most versatility in that they can set up anywhere, including a flat floor in a lab or uneven rocks on hillsides. Small footprint stand-alone units supported by the vaporizer alone can be set on truck tailgates, level ground in the middle of grassland, or an exhaust hood of a laboratory.

Large animal units are somewhat more difficult but available to mount on tripods and move to remote locations (Heath, Calkins, and Spraker, 1996). In early equine anesthesia, ambulatory units such as the Snyder and an Australian-made circuit may still be available. Some species (especially Phocid species, such as Hawaiian or Mediterranean monk seals and harbor seals) require assisted ventilation. Assist or control capability is available with bird equipment, which is fully portable and does not require electricity because it is powered by oxygen or air pressure (JD Medical, Phoenix, AZ). Patient and research needs may dictate decisions about portability. If you are working on a group of mice in the middle of an impact statement investigation, you may want to work on site, even though they are easily relocated. Likewise, if you are working on a darted 360-kg Steller sea lion on the rocks in Russia, you will have to go to the site because it is not easily picked up and moved (Figures 5.1 and 5.2).

Isoflurane or sevoflurane are the standard available agents. Halothane, although it has enjoyed many past references is less available now.

The uptake and distribution of desflurane may be desirable; however, the electrical operation and cost of the vaporizer make it less advantageous in the field. Standard anesthesia texts give appropriate pharmacological properties for investigators wanting to learn more about MAC levels, uptake and distribution, and solubility of specific agents (Hall, 1983; Lumb & Jones, 1996).

Sevoflurane has been compared to isoflurane and halothane in several species and it is advantageous in the ability to wake a wild animal up quickly and robustly, enabling a return to the environment more quickly than with isoflurane or halothane (Heath, 2000). Time is valuable in that marine mammals may return to an underwater existence in as little as 7 minutes after an hour of anesthesia (Heath, 1997, 2000; Johnson, Gelatt, and Heath, 2004).



Figure 5.1. Backpack anesthesia machine on beach in Aleutians for processing Steller sea lion puppies.



Figure 5.2. Versatile go-anywhere large animal size circuits are available on tripod mounts. Seven Seven Anesthesia, Fort Collins, CO.

Standard vaporizers are quite durable and can be packed in foam for movement. They must always be emptied prior to transport, as dangerous levels of 32% isoflurane can be delivered to the anesthetic system and patient if delivered from a tipped vaporizer.

Another delivery system that has been devised by Hodgson in Kansas involves a calculated syringe-type delivery of fluid Isoflurane to a known chamber size for immobilization of container-trapped species (Hodgson, 2005). This equipment is available through dealers for Jorgenson Lab equipment.

TRANSPORTATION AND PACKING ISSUES, INCLUDING OXYGEN PROBLEMS

Packing that has been field proven includes waterproof and armored cases such as the commercial "Pelican" case in which foam partitions can be customized. Simple barrels and plastic totes can be secured with bolt-on lids. Many suitable commercial units are available for extreme transport. Weight is an issue for air cargo, especially for helicopter work. Pilots ask the weight of all pieces, including you, to plan their flight. All pieces may well end up being carried by you to your fieldwork site, so plan and pack carefully (Figure 5.3)!

Equipment, if properly packed, can be moved to the most remote cliff edge or snow bank you can imagine. It is quite possible to drop cases of equipment out of helicopters into deep snow, land remotely, and hike over to set up your "surgical suite." Large boats have cranes, decks, repair shops, and holds to set up surgical shacks (Figure 5.4).

Commercial transport of this somewhat strangelooking equipment may need some explanation to commercial baggage x-ray personnel. It is prudent to allow for lost baggage by having backup equipment distributed in separate baggage pieces. Most of it will ship or go as baggage except full compressed gas tanks. Empty



Figure 5.3. Shipping containers are available in a wide variety of durable types and sizes. All should be options: air freight, helicopter, mailable, and back-packable.



Figure 5.4. Large spacious decks on seagoing vessels can accommodate surgical facilities. This shed was fully equipped with electricity and insulation in Southeast Alaska.

tanks are acceptable, and can be filled at your destination. Small tanks if needed (for extensive backpacking or transport where heavy tanks cannot be carried) can be refilled by careful cascading from a large tank similar to the practice underwater divers use to fill their tanks. Yokes can be made to adapt an "E" tank yoke to a large "G" tank thread (CGA-540). To avoid heating an oxygen tank, fill it *slowly*. You can get approximately eight to ten "E" tank partial refills from a large "G" cylinder. I have used diving air tanks to run anesthesia flow meters and vaporizers on a few occasions, but 100% oxygen is preferred for any anesthesia that involves much time or risk.

Full oxygen tanks may not be taken as personal baggage. Federal regulations provide as much as a \$5,000 fine for sneaking such things into your baggage. Oxygen often must be freighted by land or barge or purchased at your destination. Check with local welding shop locations. Presently, commercial companies whether medical or welding, fill most oxygen tanks on the same manifold. Medical oxygen is said to be filtered a bit more and/or dried to more stringent specifications. Welding oxygen in a remote situation is very adequate and safe.

MONITORING AND PATIENT CARE

Experience is necessary before tackling the wholesale masking use of potent agents in wild capture and anesthesia. Experience may only come from years of standing behind a surgical table. This is a relatively easy statement to make but it comes to fruition in the difficult field situation in which you may need to make judgments on what to do next, or make repairs and substitutions for equipment broken on the helicopter flight. Pups, most juveniles, and some adult individuals can be masked completely down to levels needed to intubate with inhalation alone. In handling adults of these same species the authors have been successful with prudent use of inhalation coupled with some pre-anesthetic use, usually of small doses of diazepam. Although midazolam has been shown to be useful in domestic species with a bit more direct receptor specificity, diazepam has been sufficient for use in the sea lion species (Heath, 1993; Haulena, Martin, and Heath, 2001; Johnson, Gelatt, and Heath, 2004). The authors in working with capture of larger individual sea lions have used 0.03 mg/kg intramuscular administration of diazepam to gently soften patients for masking. Isoflurane or sevoflurane at concentrations of 6% from commercial vaporizers with flow rates of 10 to 12 L/min have been sufficient for even these large individuals in restraint squeeze cages or boxes.

Other species also have been successfully inhalant anesthetized in field situations with similar careful and prudent use of knowledge and judgment (Lariviere, Walton, and Virgl, 2000; Machin and Caulkett, 2000; Lengger and Walzer, 2003).

A paper record is vital. Force yourself to keep good records and publish your results so we all may benefit. Many publications expect and require latitude-longitude coordinates to be included in your records, especially of wild animal work.

You can get by with fewer numbers of parameters monitored than you may be used to in your completely equipped hospital setting. Heavy hospital based 120/240 volt equipment can be replaced with rechargeable pieces, which then become dependent on your location and facility available for recharging. If you are working on a large seagoing vessel, electricity is no problem and you often can construct a relatively fully equipped hospital aboard. For operation in most of the world other than the United States, you must plan on 240-volt options, which most new versions of equipment will accept readily or use a voltage transformer/ inverter. For maximum portability and backpacking field use, battery-operated hand held units are preferred and widely available. Ambulance-type equipment has long battery life and good durability built in. I insist on pulse-oximetry and temperature as the absolute minimum. If time and cost permit, add capnography. Ambulatory ECG units are nice but do not actually add much more information than pulse SAO₂ and end-tidal CO₂. Many reputable companies, such as Surgivet (Waukesha, WI) and Matrx (Orchard Park, NY) provide excellent monitoring equipment (Figure 5.5).

Nelcor brand sensors offer a very good pulse oximeter clip suitable for a wide range of large and small tongues and noses. Reflectance sensors work well in esophageal and rectal positions for all size patients. Respironics brand capnograph and pulse ox units are



Figure 5.5. Monitoring for portability should be handheld, rechargeable, and include at the minimum: accurate record keeping, and temperature and pulse oximetry. Capnograph capability is recommended and valuable.

very portable, offer good battery life, and the end-tidal CO_2 is an advantage combined all in one unit. The supplied tongue clip is a bit small for larger patients. Liquid crystal screens are very difficult to read in bright sun. Pulse oximeter sensors rely on infrared wavelengths and must be shielded from direct sunlight.

Trust and believe in your instrumentation. Pulse and respiratory rate may vary greatly among species and ages of individuals. Once you have become familiar with a norm for your particular patient, pay particular attention to the other readings, temperature, pulse oximeter, and capnograph readings. Capture exertion can produce a great variation in initial body temperature; however, all anesthetized patients lose their central thermoregulatory ability and drift toward ambient temperature. Large individuals may be protected for a while but all eventually need monitoring and protection from either the sunny day or the freezing ice upon which they may be laying. Heat lamps are useful but require electrical sources. Hot water is difficult to supply in the field. Cold water may often be available for cooling and shade usually can be provided with tarps. Innovation may be needed in extreme field situations for you to protect your patient. Nutrition may be a factor in some situations, especially if a species is captive for a period of time in an unfamiliar habitat. Fluid balance is always a concern. I have found it difficult to reliably deliver fluids in the field for three reasons: weight problems in transporting any significant volume, difficulty in hitting a reliable vein in many wild patients, and mainly because we are often "just doing a short" procedure. We rationalize that we can get by without fluids, although we would not try that with our routine racehorse or family pet in a hospital setting. Fluid balance must be considered, especially in longer procedures. It is possible to administer adequate fluid load using intraperitoneal routes. Antibiotics and postoperative analgesics can be planned for and administered if indicated. Many exotic care practitioners also use intraosseous needles and report very satisfactory results with this route in difficult species for intravenous access.

SUMMARY

The veterinarian, as the main medical authority on a project, must insist on what is important for the patient at all times. Many simple procedures invariably take longer than predicted, especially if equipment fails or multiple groups of biologists want time with the patient. It is vital for the anesthetist to insist on teamwork and encourage scientists to hurry along. It is all too easy for non-medical graduate students and biologists, not familiar with patient care in a hospital, emergency room, surgical anesthesia sense, to luxuriate in the convenience of a non-moving wild patient in the field. There is always just one more test to perform and or photograph to take before wakening. It is also

imperative for the anesthetist to take command of your patient in recovery and follow completely through to full mobility and a "cage safe" situation. I recommend allowing the patient to choose the time for extubation with little stimulus before that voluntary moment. Recovery is a time that has become a favorite photo opportunity for the crowds of observers or the biology team to stand around to get a few photos. If this is disturbing to the recovery privacy of your patient, you should discourage posing with or petting the patient postoperatively. Finally, even though asleep, anesthesia and surgery are not restful experiences. Stress and exertion occur throughout drug interference in all patients; circulation is disrupted, organ function is put on hold, and patients have a lot of catch-up shivering to do.

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Section II Supportive Care, Monitoring, and Complications

6 Monitoring Darryl J. Heard

INTRODUCTION

Monitoring is essential for immobilization and anesthesia. Its goals are to detect physiological changes in time to correct irreversible injury, ensure adequate anesthetic depth, and assess the effectiveness of supportive care. The principles and techniques used in humans (Lake, 1994; Blitt and Hines, 1995) and domestic animals (Muir and Hubbell, 1991; Kaplan, 1992; Haskins, 1996) can be applied to many of the species encountered in zoological medicine. More research, however, is necessary to validate the accuracy, sensitivity, and reliability of monitoring equipment in nondomestic species.

The trend in human medicine for small portable or "bedside" monitoring systems (e.g., blood gas and electrolyte analyzers) and technology to measure variables not previously measured (e.g., hemoglobin saturation) offer opportunities to improve monitoring in animals. There is also an increasing capability to remotely monitor physiological variables in captive and free-living animals.

The following discussion is a comparative overview; more specific information is provided within the chapters for animal groups. I also recommend referring to veterinary anesthesia and critical care texts. Equipment and techniques for monitoring in remote areas are also covered in Chapter 45.

COMPARATIVE PHYSIOLOGY AND PHARMACOLOGY

Anesthetic monitoring requires understanding of normal and comparative physiology and anatomy, as well as the effects of immobilization and anesthetic drugs. Pharmacology is discussed in Chapter 1. There are many sources for information on physiology across the broad range of living animals. For example, in invertebrates (Ruppert, Fox, and Barnes, 2004), fish (Evans and Claiborne, 2006), amphibians (Duellman and Trueb, 1994), reptiles (Zug, Vitt, and Caldwell, 2001), birds

(King and McLelland, 1984; Whittow, 2000), and mammals (Cunningham, 2002). In addition, there are several excellent comparative physiology texts (e.g., Schmidt-Nielsen, 1984, 1997; O'Malley, 2005; Kardong, 2006).

MONITORING PLAN

Whether the animal is in the clinic or free living, monitoring always should begin with a plan. Written protocols, checklists, and data collection sheets are useful for communication and accurate implementation of plans. A completed checklist with a recognizable signature can be an important legal document also. As with all plans, however, the anesthetist must be ready to alter and adapt to change, and end the anesthesia if indicated.

Each anesthetic period should have a permanent record that can be an extension of the checklist. Minimally, it includes examination and history findings, recent or estimated body weight, drugs used, start and finish of anesthesia, endotracheal tube size, and problems encountered. Dunning (1993) and Silva and Downing (1995) are useful references for estimating weight of freeliving animals prior to induction. Ideally, the anesthetic record includes systematic recording of physiological variables. Human monitoring equipment routinely includes paper and electronic data recording systems. The latter offers the potential for transfer to electronic medical databases. Regular evaluation of the anesthetic machine (e.g., vaporizer setting and oxygen flow rate), monitors, fluids, etc. are included in the monitoring protocol.

A single person or "anesthetist" is assigned to each patient to manage monitoring and support. The human body and its senses is one of the best monitoring devices available and the most effective at preventing morbidity and mortality.

The information gathered during monitoring is most useful over time rather than a point measurement. The frequency of measurement or assessment is determined by the variable. For example, heart rate is assessed less than or equal to every 5 minutes.

PREANESTHETIC PREPARATION

When possible, animals are examined and their medical histories reviewed before induction. An accurate admission weight and subsequent daily weight measurements are essential patient care. Assessment of cardiopulmonary function is emphasized, and baseline values for respiration, heart rate, and temperature are determined for reference. Minimal diagnostic testing includes collection of blood for packed cell volume, total protein, glucose, and urea nitrogen levels (mammals). Additional diagnostic tests (e.g., hematology, plasma biochemical panel, and radiographs) are performed as indicated.

Free-living or aggressive animals are examined immediately post-induction. Preinduction visual examination of these animals may reveal open-mouthed breathing, tachypnea, dyspnea, nasal discharge, altered mentation, abnormal mucous membrane color, cachexia, or signs of dehydration. These clinical signs may be indications to alter or cancel immobilization or anesthesia.

ANESTHETIC DEPTH

Depth is determined by the drugs, dosage, species, presence or absence of disease, and physiological status. Cross-species assessment is facilitated by subdividing anesthesia into unconsciousness or amnesia, analgesia, and muscle relaxation (Haskins, 1996). The presence of adequate muscle relaxation, however, does not necessarily imply unconsciousness or analgesia (e.g., muscle relaxants).

Unconsciousness is based on anesthetic dosage or vaporizer setting, muscle relaxation, decreased reflex activity, and absence of limb movement. Electroence-phalography has been evaluated in research (e.g., cetaceans, Chapter 43) and some domestic animals. Unfortunately, this technology is not available for routine use or has not been validated in nondomestic animals.

Increasing depth is assumed when muscle tone (e.g., jaw muscle or anal sphincter) decreases, palpebral and corneal reflexes are obtunded, and respiration pattern becomes regular and even. Corneal reflex and anal tone are usually present at surgical anesthetic levels. Palpebral and corneal reflexes are not elicited in snakes and some lizards because their eyelids are fused into a spectacle covering the cornea. Similarly, fish do not have eyelids. These reflexes are also difficult to assess in small animals because of ocular size. A Q-tip can be used to gently touch the eyes. In mammals eye position often changes with anesthetic level. This change can be validated as anesthesia is deepened and lightened. In vertebrates a fixed dilated pupil, unresponsive to light and with no corneal reflex, is an indication of excessive depth or brainstem ischemia. In an anesthetized bird sudden erection of the feathers is a reflection of cardiac arrest or hypoperfusion, not awakening.

Pain is the conscious perception of nocioception, the activation of specialized receptors in response to a noxious stimulus (see Chapter 3). All animals are assumed to have nociceptors and potentially able to perceive pain. Pain and nociceptor response are assessed by evaluating physiological and muscular response to a stimulus. Care is taken to provide a stimulus reflective of surgical pain that does not traumatize tissues. This can be a toe, an ear, cloacal (in reptiles) or tail pinch, a skin incision, feather plucking (in birds), or visceral manipulation (during a laparotomy). In lower vertebrates the stimulus should be applied for several seconds to allow for a delayed response. Plucking a bird's feathers can be more painful than a skin incision.

A surgical plane is assumed when no muscle movement occurs and physiological changes are minimal or absent. Sudden tachycardia, hypertension, or tachypnea in response to stimuli indicates inadequate depth or analgesia. Appropriate responses include stopping the painful stimulus, graded increases in anesthetic dose (e.g., increased vaporizer setting), or parenteral administration of an analgesic, usually an opioid (see Chapter 3). Although most inhalant anesthetics produce unconsciousness, they are poor analgesics. An exception is nitrous oxide, but it does not produce unconsciousness.

Inhalant anesthesia is the basis for most small animal regimens. Minimum anesthetic concentration (MAC), or dose (MAD) in birds (Ludders, Mitchell, and Schaefer, 1988; Ludders, Rode, and Mitchell, 1989), is a measure of inhalant anesthetic potency (see Chapter 1). MAC is the anesthetic concentration (volume%) that produces immobility in 50% of an anesthetized populations subjected to a noxious stimulus (Quasha, Eger, and Tinker, 1980; Ludders, Mitchell, and Schaefer, 1988). Knowledge of the MAC value in one species is used to approximate vaporizer settings for surgical anesthesia in other species. MAC is similar within and across animal classes (Quasha, Eger, and Tinker, 1980). Maintenance surgical anesthesia vaporizer settings are approximately 25% higher than MAC. For example, the measured MAC of isoflurane usually lies between 1.5% and 2.0%, whereas maintenance vaporizer settings range from 2.0% to 2.5%.

Hypothermia decreases MAC (Quasha, Eger, and Tinker, 1980). In poikilotherms (i.e., reptiles, amphibians, fish) patients with a body temperature lower than their preferred optimum require a lower maintenance anesthetic setting. Although less dramatic, similar effects are observed in hypothermic (and possibly hibernating) birds and mammals. Premedication with opioids and other premedicants also decrease MAC. For example, butorphanol (1 mg/kg) reduced MAD in cockatoos by 25% (Curro, Brunson, and Paul-Murphy, 1994).

MAC does not predict induction and recovery time because it is measured when inhalant concentration in the respiratory tract has equilibrated with the central nervous system. They are primarily determined by inhalant anesthetic tissue and blood solubilities, ventilatory efficiency, and circulation time. Hence, isoflurane induction is more rapid than with halothane because of its lower blood and tissue solubilities. Reptiles have longer induction times than do mammals and birds because of inefficient respiratory systems and slow circulation times. Another factor in reptiles, particularly aquatic and semiaquatic species (i.e., crocodilians and chelonians), and amphibians, is the presence of cardiac shunts. These shunts bypass perfused pulmonary tissue, delaying inhalant anesthetic induction and recovery.

During inhalant induction snakes generally relax from head to tail and recover in the opposite direction. The absence of a response to a cloacal pinch is suggestive of an adequate surgical plane of anesthesia. Similarly, the toe pinch response is used to monitor anesthetic depth in lizards, crocodilians, tortoises, and turtles. The palpebral or corneal response is used in crocodilians, tortoises, turtles, and most lizards. A classification system for assessing anesthetic depth in avian patients has been described (Arnall, 1961). Anesthetic depth in birds and small mammals is assessed using the pinch response, palpebral and corneal reflexes, eye position, jaw tone, respiration rate and depth, and heart rate response.

CARDIOVASCULAR MONITORING

Anatomy and Physiology

Amphibian and most reptilian hearts are composed of three chambers: two atria and one ventricle (White, 1976). The single ventricle functionally acts as two ventricles, with a variable amount of right-to-left shunting. Increased shunting bypasses the lungs with decreased systemic arterial oxygenation. Crocodilian, avian and mammalian hearts are composed of four chambers: two atria and two ventricles. However, crocodilians also can shunt blood from right to left through a vascular foramen (White, 1976).

Vertebrate hearts are located on or slightly to the side of midline in the cranial third of the body cavity. The ventricle(s) are directed between ventral and caudal, and between midline and left lateral. In lizards, cardiac location varies from between the forelimbs (e.g., iguanas, chameleons, skinks, and bearded dragons) to almost the middle of the body (e.g., monitor lizards, tegus) (Murray, 1996). In snakes, cardiac position is influenced by the predominant lifestyle: The distance from heart to the head is ranked arboreal < terrestrial < aquatic (Lilywhite, 1996). Cardiac location is determined by turning the snake and visualizing the movement of the ventral scales over the heart associated with cardiac contraction. This is facilitated by light reflecting off the scales. The avian heart is enveloped by the liver lobes and protected ventrally by the wide flat sternum. The mammalian heart (left ventricle) extends cranially from

the point at which the left elbow lies over the costochondral junction.

Reptilian, avian, and mammalian heart rates are primarily determined by temperature, size, metabolism, respiratory state, and the presence or absence of painful stimuli (White, 1976). Hypothermia is most important in amphibians and reptiles because of the wide range of body temperatures encountered. Heart rate is inversely related to body size (Schmidt-Nielsen, 1984). The resting heart rate (min⁻¹) for mammals is calculated from the allometric equation:

$$241 \times M_b^{-0.25}$$

where M_b = bodyweight (kg) (Schmidt-Nielsen, 1984). The equation for birds is

$$155.8 \times M_b^{-0.23}$$
.

A heart rate 20% above or below the calculated rate for an individual patient is considered to be either tachycardic or bradycardic, respectively (Sedgwick, 1991).

Principles of Cardiovascular Monitoring

The main function of the cardiovascular system is oxygen (O₂) and nutrient delivery to tissue cells, and carbon dioxide (CO₂) and waste (e.g., lactate) removal. Adequate cardiovascular function implies sufficient capillary flow to fulfill these functions. Unfortunately, no reliable, accurate, and effective way to measure capillary flow exists. Although cardiac output can be measured, it is not feasible for routine monitoring in veterinary practice. Systemic arterial pressure measurement provides an indirect assessment of cardiac output and, by extension, tissue perfusion. Increased peripheral resistance (e.g., increased arteriolar tone in response to epinephrine) results in apparently adequate systemic arterial blood pressure (i.e., in mammals a mean arterial pressure equals 60 mmHg), but decreased or absent capillary blood flow to one or more tissue beds (e.g., kidneys or gastrointestinal tract). Other indirect indicators of peripheral perfusion include capillary perfusion time, mucous membrane color, urine production, and blood gas analysis. Heart rate is one determinant of cardiac output; therefore, marked tachycardias, bradycardias, and arrhythmias (e.g., ventricular tachycardia, fibrillation, and third-degree heart block) can decrease flow.

Auscultation

Auscultation is used to determine heart rate and rhythm and to detect and assess the presence of cardiac murmurs. Heart sounds usually are not auscultable in amphibians and reptiles. In birds, the large pectoral musculature and broad sternum obtund the cardiac sounds. Avian and mammalian hearts are auscultated on either side of the chest and at the thoracic inlet.

The esophageal stethoscope is an inexpensive, simple monitor of heart and lung sounds. It consists of a catheter fitted with openings in the distal 2 to 3 cm,

which are covered by a rubber cuff. More sophisticated versions incorporate electrocardiography (ECG) electrodes. An esophageal stethoscope can be used during all anesthetic procedures in which the patient is intubated. Alternatively, a high-quality pediatric stethoscope is usually available for immediate use.

Esophageal stethoscope placement is difficult in birds with complex crops (e.g., parrots and pigeons). The lubricated tube is passed down the esophagus on the right side of the neck until it reaches the crop. The tip is then palpated through the crop wall and directed to the midline to pass through the thoracic inlet into the thoracic esophagus. The esophageal stethoscope is best placed soon after anesthetic induction, rather than during an emergency. It is impractical to use an esophageal stethoscope in small patients, and it can induce regurgitation in guinea pigs.

Capillary Refill Time

Capillary refill time is an indirect measure of peripheral tissue perfusion. Concurrent assessment of mucous membrane and skin color can indicate anemia (pallor), endotoxemia (hyperemia then pallor), and hypoxemia (blue or purple). Interpretation of mucous membrane color must allow for the diversity of normal pigmentation. The tongue tip of many iguanid lizards is a dark red.

Anesthetic drugs affect interpretation of color and refill time; α -2-adrenergic agonists produce intense peripheral vasoconstriction and pale mucous membranes. Similarly, hypothermia and hypovolemia or hypotension produces vasoconstriction. Inhalant anesthetics can produce an initial vasodilation and apparent congestion of mucous membranes and skin (e.g., reddening of the facial patches in macaws). Although normally pale, reptile mucous membranes become congested when the head is placed lower than the body or the neck is compressed by constrictive bandages.

To determine capillary refill time, the mucous membrane of the oral cavity is digitally compressed until blanched, and the time it takes to return to its original color is determined. This time should be 2 seconds or less in birds and mammals; a prolonged capillary refill time is indicative of poor peripheral tissue perfusion.

Electrocardiography

ECG monitoring is indicated for routine monitoring and whenever an abnormal pulse or arrhythmia is detected or the history suggests the possibility of an arrhythmia (e.g., syncope) (Figure 6.1). The ECG should have a multichannel oscilloscope with nonfade tracing and freeze capabilities. Also, it must be able to record at speeds of 100 mm/s and amplify the signal to at least 1 mV equal to 1 cm. The ECGs of mammals, birds, reptiles, amphibians, and fish resemble each other in general form, with clearly defined P, QRS, and T components. In reptiles, an SV wave can be observed preceding



Figure 6.1. An Amur leopard anesthetized for surgery of an obstructed section of bowel. Multiple monitoring modalities are being used to assess physiological function including thoracic auscultation, an electroencephalogram, pulse oximetry, capnography, and direct and indirect blood pressure measurement. Some, or all, may be used in free-living animals depending upon availability and portability.

the P wave (White, 1976). In fish, a V wave may precede the P wave, whereas a B wave indicates depolarization of cardiac muscle in the conus arteriosus of sharks (Olson and Farrell, 2006).

Standard lead positions described for cats and dogs are used for mammals, birds, and reptiles (Figure 6.1). Traditional positioning does not provide adequate wave deflections in reptiles and low signal voltages. Electrodes are placed in the cervical region in lizards with hearts located at the pectoral girdle (Murray, 1996). In snakes, the electrodes are placed two heart lengths cranial and caudal to the heart (Murray, 1996). In tortoise and turtles, the cranial leads are placed on the skin between the neck and the forelimbs (Murray, 1996). To improve signal detection, stainless steel suture is passed through the skin and attached to the electrodes. In birds, electrodes are attached to the prepatagial regions of the wings and on the medial thigh regions.

Doppler Flow Detection

Doppler flow detection is used for audible monitoring of blood flow in unconscious or cardiovascularly unstable animals (Figure 6.2). It is based on the Doppler principle: The frequency of transmitted sound waves is altered when reflected off moving red blood cells (Crowe and Spreng, 1995). The magnitude and direction of the frequency shift are related to the velocity and direction of the cells and are converted into an audible sound. The Doppler flow detector uses a probe placed as close as possible to blood flow in an artery or the heart. The probe contains the high-frequency sound transmitter and the receiver. Three types of probe exist: (1) human adult; (2) pediatric; and (3) pencil. The pencil probe has a small probe surface at the end of an



Figure 6.2. An anesthetized koi. Cardiac blood flow is being assessed with a pencil Doppler flow probe.

elongated holder and is valuable for assessing blood flow in small patients (Figure 6.2).

Decreases in volume indicate a decrease in blood flow or displacement of the probe. As with all monitoring equipment, the animal always should be checked first when the Doppler does not seem to be working. The Doppler is used wherever major arteries are close to the skin. In mammals and reptiles, contact sites include the ventral aspect of the tail base; the carotid, femoral, and auricular (mammals) arteries; and directly over the heart (Figure 6.2). In birds, contact sites include the ulnar, metatarsal, and carotid arteries. In reptiles, the lubricated Doppler probe can be turned dorsally and inserted into either the esophagus or cloaca to detect blood flow. In large reptiles (and other vertebrates) the probe also can be placed over the eye to detect ophthalmic arterial blood flow. In turtles and tortoises the pencil probe is placed at the thoracic inlet to detect cardiac flow.

Arterial Blood Pressure Measurement

The mean arterial blood pressure is a better indicator of tissue perfusion than systolic or diastolic pressure. The two forms of systemic blood pressure measurement are indirect and direct.

Indirect Blood Pressure Indirect measurement is least accurate and most appropriate for physiologically stable patients. The three main techniques used are

oscillometric, automatic, and Doppler (Kaplan, 1992; Crowe and Spreng, 1995). The oscillometric technique uses a manometer within the occlusion cuff to detect oscillations of the encircled artery (Figure 6.1). As cuff pressure increases to more than systolic pressure, arterial blood flow ceases. As cuff pressure slowly decreases to less than systolic pressure, intermittent blood flow is detected as needle oscillations on the manometer roughly corresponding to the mean arterial pressure. Diastolic pressure is read at the point at which needle oscillations no longer decrease in magnitude and is the least accurate of the three measurements. The automatic technique uses the same methodology as the oscillometric technique, except that the cuff is inflated and deflated automatically.

With the Doppler technique, as cuff pressure slowly decreases and pulsatile arterial blood flow begins, an audible Doppler signal is detected corresponding to systolic arterial pressure. Diastolic arterial blood pressure is indicated by an abrupt muffling or cessation of sound as the vibrations of the arterial wall ceases.

Sites for indirect blood pressure measurement include the legs (Figure 6.1), tail, and ears (in rabbits). Indirect measurement is least accurate at low systemic pressures and when small arteries are used. One must have the appropriate cuff size; its width should be approximately 40% of the circumference of the limb (Crowe and Spreng, 1995). Narrow and wide cuff widths provide erroneously high and low pressure measurements, respectively.

Direct Blood Pressure Direct arterial blood pressure measurement is used less frequently than indirect because it is technically difficult and requires an expensive monitor. It is feasible, however, in large mammals and birds. It is easily performed in rabbits because of the accessible auricular artery in the center of the pinna. Similar arterial access exists in many other mammals with large ears (Figure 6.3); the extreme example is the elephant. In birds weighing greater than or equal to 1 kg arterial catheters are placed percutaneously in the ulnar or the dorsal metatarsal artery (see Chapter 22). The advantages of direct blood pressure measurement are it gives a constant reading and the catheter can be used as a source of arterial blood for gas analysis.

Central Venous Pressure

The central venous pressure (CVP) reflects intravascular volume, cardiac function, and venous compliance. Its measurement is indicated in patients with marginal cardiac function, with decreased glomerular filtration rate, or those receiving large volumes of fluids. Although not commonly used, it can be determined whenever a jugular catheter tip extends close to the junction between the cranial vena cava and the right atrium (Kaplan, 1992). A three-way stopcock is attached to the jugular catheter to the administration set of the animal's



Figure 6.3. An anesthetized gerenuk. An over-the-needle 20-gauge catheter is being placed in an auricular artery for direct arterial blood pressure measurement and collection of samples for blood gas analysis. Infiltration of the periarterial tissue with 2% lidocaine dilates the artery and blocks vasospasm, facilitating catheter placement. A pulse oximetry probe has been placed on the tongue for hemoglobin saturation measurement. An in-line capnometry probe is attached to the end of the endotracheal tube for end-tidal carbon dioxide measurement.

intravenous fluids, and to a vertically positioned manometer. The manometer is zeroed to the level of the right shoulder (sternal recumbency) or center of the thoracic inlet (lateral recumbency). When the manometer is filled from the fluid bag and the stopcock is opened to the jugular catheter, the fluid in the manometer slowly drops and levels out at CVP. This procedure is repeated at least three times and the average recorded in cm $\rm H_2O$. Single CVP measurements do not reflect an animal's hemodynamic status; changes with time are most important. Normal mammalian CVPs range from 0 to 5 cm $\rm H_2O$.

Dehydration

Determination of relative hydration involves integration of data from several sources, including history, physical examination, and blood work. Although skin tenting is emphasized in domestic animals, it is difficult to interpret in nondomestic animals given the wide range of skin types. Gently grasping a fold of skin and rolling it between fingers is a more reliable technique. Normally hydrated skin moves easily, whereas in dehydrated animals, a "sticky" feeling exists. Dehydration also produces dry mucous membranes, sunken eyes, and

decreased tear production. The packed cell volume (PCV), total protein level, plasma osmolality, and electrolyte concentrations often are increased. The urine specific gravity usually is increased, and urine production usually is decreased. Dehydration is graded as mild (2% to 4%), moderate (6% to 8%), or severe (10% to 12%).

RESPIRATORY MONITORING

Auscultation

As with cardiac auscultation, evaluation of the respiratory system requires a good-quality stethoscope with appropriate head and length of tubing and an experienced ear. The esophageal stethoscope can be used to evaluate respiratory noise. However, artifactual noise must be distinguished from true respiratory noise.

Blood Gas Analysis

Arterial blood gas analysis assesses patient oxygenation, acid-base status, and adequacy of ventilation. Venous blood gas samples are more easily obtained than are arterial samples, but interpretation is difficult. They reflect arterial $\rm CO_2$ and $\rm O_2$ levels only crudely, and are affected by local tissue metabolic activity and low blood flow. Cardiocentesis blood gas samples in turtles (Kerr and Frankel, 1972) and other reptiles are not an accurate reflection of systemic (i.e., carotid) arterial values because of intracardiac shunting. Arterial blood gas analysis is used periodically to assess the accuracy of pulse oximetry or capnography during surgery.

Blood gas values are corrected to the patient's body temperature or analyzed at a standardized temperature. Selection of a technique to use is controversial, particularly in ectothermic animals (Wang, Smits, and Burggren, 1998). When using either technique it is important to review reference values for the species when available.

Arterial blood gas samples are obtained from any palpable artery. Collection sites include the femoral, metatarsal (see Figure 6.1), ulnar (birds, Chapter 22), carotid, digital, and auricular arteries (Figure 6.3). Infiltration of the periarterial area with 1% lidocaine without epinephrine can prevent reflex vasospasm. Samples are collected into heparinized 1- or 3-mL syringes through a 25- or 27-gauge needle. After collection, all air is evacuated from the syringe, a cork placed on the needle, and the sample processed as soon as possible. The sample syringe is placed in crushed ice if the time between collection and analysis is prolonged. Avian and reptile red blood cells have a high metabolic activity, so that immediate sample processing is recommended (Wood, 1976). There are several portable blood gas analyzers available that use small blood volumes. For example i-STAT (Abbott Point of Care Inc., East Windsor, NJ) and IRMA Trupoint Blood Analysis System (ITC, Edison, NJ).

Pulse Oximetry

Pulse oximetry is indicated for monitoring blood oxygenation and controlling O_2 administration. The latter allows for administration of the lowest concentration of inspired O_2 compatible with safe levels of arterial oxygenation. Commercial pulse oximeters also measure pulse rate.

Pulse oximeters estimate arterial hemoglobin O₂ saturation (SaO₂) by measuring pulsatile signals across (transmission) or by reflectance (reflection) from perfused tissue at two discrete wavelengths (660 nm, red; 940 nm, infrared) using the constant component of absorption (i.e., that caused by everything except arterial blood) at each wavelength to normalize the signals (Tremper and Barker, 1994; Schmitt, Göebel, and Trautvetter, 1998). A ratio (R) between these two normalized signals is calculated and related to arterial O2 saturation using an empiric algorithm. This R value varies from 0.4 to 3.4 over the saturation range of 0% to 100%. All commercially available pulse oximeters calculate hemoglobin saturations from algorithms developed by measuring the R in human volunteers and simultaneously sampling arterial blood for in vitro saturation measurements (Tremper and Barker, 1994). An R of 1.0 corresponds to a pulse oximeter saturation reading (SpO₂) of approximately 85% (Tremper and Barker, 1994).

Potential sites for placement of transmission pulse oximeter sensors include the ear, tongue (Figure 6.4), buccal mucosa, paw, vulva, prepuce, and tail. A reflectance pulse oximeter sensor is used in the esophagus, rectum, or cloaca. Surprisingly, the best site in rabbits is the base of the tail rather than the ears, which could be because of excessive compression of the aural vasculature. Pulse oximeters require adequate plethysmographic pulsations to allow them to distinguish arterial light absorption; therefore, they are inaccurate in the presence of decreased blood pressure, decreased pulse pressure, and vasoconstriction. The oximeter measures a pulse but not peripheral perfusion (Tremper and Barker, 1994). The presence or absence of a pulse is quickly detected, but the presence of a pulse does not ensure adequate blood flow.

Pulse oximeter calibration assumes only two hemoglobin types in the bloodstream: (1) oxyhemoglobin; and (2) hemoglobin. If methemoglobin or carboxyhemoglobin is present, it is interpreted as oxyhemoglobin, hemoglobin, or some combination of the two (Tremper and Barker, 1994). High methemoglobin levels force SpO₂ toward 85% regardless of PaO₂ and SaO₂ values.

The accuracy and reliability of pulse oximeters also varies among domestic mammal species, probe position, and commercial brands (Matthews, Hartke, and Allen, 2003). Not surprisingly, this variability extends to nondomestic mammals and their use in birds, reptiles, and other vertebrate groups is even more controversial.

Schmitt, Göebel, and Trautvetter (1998) evaluated two pulse oximeters, the Pulsox 7 and the Oxycount



Figure 6.4. An anesthetized white-handed gibbon. A pulse oximetry probe has been placed on the tongue for monitoring hemoglobin saturation.

Mini (Andos, Hamburg, Germany) in pigeons, macaws, and African gray parrots. SpO_2 values were compared with SaO_2 values calculated from ulnar PaO_2 using a published pigeon O_2 hemoglobin dissociation curve. The probes were positioned over the gastrocnemius and tibialis cranialis muscles. The study demonstrated a different photometric behavior for avian and human hemoglobin, which would be expected to result in an underestimation of saturation values in birds. Saturation values recorded by pulse oximetry did not correlate well (R=0.81) with calculated SaO_2 values. The investigators concluded that pulse oximetry is unsatisfactory for routine use in birds. Additional research is necessary to develop an avian calibration curve for pulse oximetry.

Diethelm, Mader, and Grosenbaugh (1998) evaluated pulse oximetry in green iguanas. Oxyhemoglobin and deoxyhemoglobin absorbencies at 660 and 940 nm were determined in vitro to be similar to human hemoglobin. Although iguana hemoglobin seemed to absorb more light at 660 nm than did human hemoglobin, it was thought to be a preparation artifact. Six anesthetized iguanas were administered inspired O2 concentrations of 7%, 10%, 20%, and 100%. A reflectance probe was placed in the esophagus and the measured (SDI Vet/Ox 4402, Sensor Devices Inc., Waukesha, WI) SpO₂ values were compared with SaO₂ values calculated from PaO₂ values of blood samples obtained from the abdominal aorta. No significant differences were found between SpO₂ and SaO₂ values, and the investigators concluded that pulse oximetry is an excellent tool for monitoring pulse rate and oxygen saturation in iguanas. The study abstract (Diethelm and Mader, 1999) does not mention how the SaO_2 values were calculated. In green iguanas Mosley, Dyson, and Smith (2004) found no correlation between pulse oximetry and calculated hemoglobin saturations. Additional research is necessary

to evaluate pulse oximetry in all groups of nondomestic animal.

Capnography

Capnometry is the measurement of CO₂ concentrations in expired gases (Gal, 1994); capnography refers to the display of these concentrations on an oscilloscope screen or recording chart, usually as a function of time. Carbon dioxide is monitored by direct inline measurement at the sample site by a flow-through device (Figures 6.1 and 6.3) or aspiration of the gas sample into a separate monitor. In-line sensors are fragile, expensive, cumbersome, and have a relatively large dead space (Gal, 1994). Analyzers that continually withdraw gas samples are plagued by excess moisture and require that the small-diameter sampling tube be as short as possible to improve response time (Gal, 1994).

End-tidal CO_2 tension (PETCO₂) is used to provide a noninvasive estimate of $PaCO_2$. In birds, however, with their unique respiratory system and air-flow patterns the PETCO₂ can be higher than $PaCO_2$ (Edling, Degernes, and Flammer, 2001). Lung disease increases the difference, as can sample errors. The most obvious sampling error is a system leak. Another sampling problem is related to the sampling rate and the minute ventilation of the patient. When used in small patients, high sampling rates (i.e., 250 ml/min) can result in entrainment of room air and lower PETCO₂ values. In human pediatric patients, the sampling rate is set at 50 mL/min. This rate is still too high in many small patients.

TEMPERATURE MONITORING

Body temperature measurement is a standard of care during all anesthetic procedures (see Chapter 9). Hypothermia is common in small anesthetic patients because of the large surface area-to-volume ratio. Also many drugs used in the perianesthetic period suppress normal thermoregulatory mechanisms. The anesthetic gases used during inhalation anesthesia are of low humidity and temperature. Hyperthermia is also common in the period immediately after immobilization of both captive and free-living mammals and birds.

Thermometers should not be made of glass because of the risk of breakage and injury. They should be able to read over a wide temperature range, especially for use in ectothermic animals. Digital thermometers are useful if they have a short measurement time.

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7

Cardiovascular and Pulmonary Support

Craig Mosley and Cornelia Gunkel

GENERAL

Anesthesia-related complications are not uncommon and can lead to peri- or post-anesthetic difficulties. Complications may be related to inappropriate use of equipment, adverse drug effects, inadequate patient support (cardiovascular and respiratory) and preparation, inherent patient factors such as regurgitation, or complex multifactorial pathological processes such as myopathy or neuropathy. Without appropriate monitoring and critical follow-up, some problems remain unnoticed and may only be recognized as unexplained morbidity following anesthesia (Dyson, Maxie, and Schnurr, 1998). Occasionally complications are obvious and need immediate treatment to prevent mortalities. Most complications are related to interactions among the drugs administered, the underlying physiological and pathophysiological condition of the animal or related to the fact that adequate monitoring and/or cardiovascular and pulmonary support for the animal were not provided during anesthesia. Dramatic improvements in anesthetic care can be realized by applying standard principles of monitoring and supportive care. However, it is important that the individual charged with monitoring clearly understand the information the monitor is providing. It should be recognized that it is the anesthetist that is responsible for interpreting monitored values and ultimately responsible for monitoring the patient. Anesthetic monitors do not, by themselves, monitor and manage the anesthetized patient.

This chapter provides an overview of how to treat common cardiovascular and respiratory complications under general anesthesia. General principles are discussed. A detailed species-specific description of complications is not possible. However, by combining sound treatment principles and an understanding of species-specific physiological differences and similarities most complications in all species can be approached and managed logically.

CARDIOVASCULAR

The cardiovascular system is essential for maintaining blood flow to tissues, transporting oxygen and nutrients to meet tissue metabolic needs, and removing carbon dioxide and wastes. Unfortunately, most anesthetic drugs also variably depress this essential body system. Minor cardiovascular abnormalities (e.g., mild dehydration, hypovolemia, sepsis, mild cardiac disease, etc.) can be markedly exaggerated in the anesthetized patient. Anesthesia obtunds many of the normal compensatory effects of the cardiovascular system, leading to exaggerated cardiovascular responses under anesthesia (Hellyer et al., 1989; Van Leeuwen, Evans, and Ludbrook, 1990). This is especially problematic in most non-domestic animals, in which physical and laboratory examinations are limited; therefore, close monitoring during anesthesia is essential. Recognition of abnormalities and trending can help identifying potentially detrimental alterations as early as possible so that appropriate adjustments to the anesthetic regimen can be made or additional support can be provided to prevent catastrophic complications from developing. Identification of underlying abnormalities should begin immediately following premedication/induction and continue until full recovery has occurred.

The best monitoring equipment are those that are easily transportable for the field, but robust enough and capable of providing the information needed to properly assess the cardiovascular status of the patient. In general blood pressure is one of the most useful cardiovascular parameters to evaluate. It provides indirect quantification of blood flow and tissue perfusion. Some instruments such as a Doppler produce continuous, audible information and give some indication of heart rate and rhythm (Nicholson, 1996; Hall, Clarke, and Trim, 2001). Please see the appropriate chapters (in this text) for more detailed discussion on monitoring equipment.

Intravenous Fluid Therapy

Intravenous fluids are an important means of providing cardiovascular support and even for the shortest procedure it is generally best to place an intravenous catheter (if size and anatomy of the animal allow). Most anesthetics (particularly inhalants) reduce myocardial contractility, cardiac output, vascular responsiveness (baroreceptor response), and can cause vasodilation (Steffey and Howland, 1977). These alterations can lead to a reduction in arterial blood pressure, increased intravascular volume (resulting from vasodilation), and a reduction in tissue perfusion, predisposing to complications (e.g., myopathy). In addition to counteracting the hemodynamic effects of general anesthetics, intravenous fluid administration provides a route for the administration of emergency drugs and intraoperative support and can be used to replace fluid losses associated with surgery. This increases safety for the patient and personnel, particularly if an unexpected awakening occurs.

Fluids administration is strongly recommended for all anesthetized animals when possible, especially when the hydration status is unknown or questionable, the ambient temperature is high, or the induction was stressful and prolonged.

Many different fluid types are available. In general a balanced electrolyte solution is suitable in most situations. Modification of fluid administration protocols is influenced by species, concurrent disease (e.g., cardiac, pulmonary, cerebral, or renal), hydration, and electrolyte status as well as ongoing losses (e.g., bleeding, sweating).

Several types of fluids are available for fluid therapy (Matthews, 1998; DiBartola and Bateman, 2006). Some of the common fluid types are described in the following.

Crystalloids Crystalloids are solutions containing water, electrolytes, and other small solutes (e.g., glucose). Crystalloids are frequently classified as replacement or maintenance solutions. Replacement solutions have electrolyte compositions similar to extracellular fluid or plasma and are isotonic. These solutions are most commonly used for the replacement of fluid deficits associated with hypovolemia and dehydration (Matthews, 1998). Maintenance solutions have electrolyte compositions appropriate to replace daily sensible and insensible losses. These solutions are often hypotonic and tend to have lower sodium and higher potassium concentrations than replacement solutions. These fluids generally are not suitable for fluid therapy during anesthesia because of the potential for potassium overdose and inappropriate electrolyte composition. Crystalloid fluids are also described based on their tonicity; hypotonic, isotonic, and hypertonic.

Hypotonic Crystalloids Hypotonic crystalloids are rarely used for perianesthetic fluid support. Generally these fluids are used as maintenance solutions; they distribute to both the extracellular and intracellular fluid compartments and may precipitate the formation of edema if large quantities are used.

Isotonic Crystalloids Isotonic crystalloids are the most common fluid for supportive therapy during anesthesia. They are frequently used to increase intravascular volume, offsetting some of the hemodynamic changes associated with anesthesia. However, it is important to recall that approximately 75% of the administered volume is redistributed to the interstitial space, less than 20% remains in the intravascular space after 2 hours, and about 10% remains after 3 hours (Shoemaker et al., 1981; Hahn, Drobin, and Stáhle, 1997). Crystalloid solutions can be alkalinizing or acidifying, this effect depends on added base precursor (e.g., lactate or acetate) and the strong ion difference of the solution. Lactate is a mild alkalinizing agent when metabolized in the liver. Acetate does not require liver metabolism to exert its alkalinizing effects (Matthews, 1998). Several isotonic crystalloids contain calcium that can bind the anticoagulant, citrate, in stored blood products and may lead to coagulation if they are administered in the same line as blood or plasma (Ryden and Oberman, 1975). Sodium bicarbonate may also precipitate in calcium-containing solutions. In neonates and patients with impaired hepatic function isotonic crystalloids are often supplemented with glucose (i.e., 2.5% dextrose).

Recommended administration rates are: shock rate (for rapid resuscitation), 45 to 90 ml/kg/hour; anesthesia maintenance rate, 5 to 20 ml/kg/hour. These rates are guidelines and should be adjusted to reflect individual requirements. Blood pressure, heart rate, capillary refill time, and serial packed cell volume (PCV), total protein (TP), and lactate assessment can be used to help guide therapy.

Hypertonic Crystalloids Hypertonic crystalloids are occasionally used for emergency resuscitation of hypovolemic patients. The most commonly used is 7.2% NaCl with an osmolarity of approximately 2,400 mOsm/L. Following the administration of hypertonic saline, fluid is pulled from the extravascular to the vascular space increasing plasma volume (approximately 5× infused volume). The effect on vascular expansion is transient (30 to 60 minutes) because of redistribution of the NaCl in the extracellular space and urinary losses (Mazzoni et al., 1988). Appropriate isotonic crystalloid, based on deficits, should be administered following hypertonic saline administration to maintain intravascular volume and to prevent exacerbating dehydration (Matthews, 1998). Recommended doses are 2 to 8 ml/kg of hypertonic saline administered over 15 minutes.

Colloids Colloids are aqueous solutions containing macromolecules that do not normally pass through the capillary membrane. Colloids are used to maintain intravascular fluid volume and are useful when large

volumes of crystalloid are unavailable or patients require oncotic therapy (e.g., hypoproteinemia). Colloids can be classified as synthetic (complex carbohydrate preparations) or natural (albumin containing blood products). Synthetic colloids include dextrans, hetastarch, and pentastarch. Synthetic colloids are eliminated by glomerular filtration, extravasation, storage in tissues, and the gastrointestinal tract (Matthews, 1998).

All colloids can potentially impair coagulation via a direct effect on platelets and clotting factors as well as indirectly by inducing a mild dilutional coagulopathy (Concannon, 1993; Kirby and Rudloff, 1997). Dextrans tend to have the greatest effect on coagulation when compared with hetastarch and pentastarch. Precautions for using synthetic colloids include patients with anuric or oliguric renal failure, congestive heart failure, pulmonary edema, and intracranial hemorrhage. Intraoperative maintenance rates range from 2 to 4 ml/kg/hour with the usual recommended daily (24-hour) dose being less than 20 ml/kg. Colloids interfere with total solid readings from a refractometer making assessment of total solids less useful (Bumpass, Haskins, and Kass, 1998).

Natural Colloids Natural colloids include all plasmabased products providing colloidal support (whole blood and plasma). Blood transfusions are often not possible or difficult to perform in many non-domestic species (Lichtenberger, 2004). Not only is the procedure for collecting blood from a donor animal potentially difficult and dangerous but little is known about blood types and cross-reactions among these animals. Lifethreatening reactions are possible even with the first transfusion if the species has naturally occurring alloantibodies against non-self blood antigens. For example, the domestic cat has naturally occurring alloantibodies to non-self blood and hence a mismatched transfusion even in a naïve animal can lead to life threatening reactions (Griot-Wenk and Giger, 1995). Whole blood transfusions are indicated for hemorrhagic shock, coagulation disorders, hemolytic crises, and nonresponsive anemias. The decision to begin a transfusion should be based on an assessment of the specific deficit (red blood cells, platelets, etc.), the cause of the deficit, duration over which the deficit developed, physical examination, and laboratory examination findings. Although there are no definitive guidelines for transfusions, some general recommendations follow: blood loss approaching 20% to 30% of total blood volume or a PCV less than 12% (Prittie, 2003). Plasma transfusions are indicated for restoration of plasma oncotic pressure (hypoalbuminemia) and coagulation disorders (fresh or fresh-frozen only). Plasma transfusions are likely to be less associated with reactions as very little red cell antigen is present in well-prepared plasma; however, non-antigenic serum reactions are possible (Kudnig and Mama, 2002). Once again there are no specific guidelines for determining the need for a plasma transfusion. However the authors routinely use a total plasma protein less than 35 g/L or serum albumin less than 15 g/L. All blood products should be administered through an appropriate administration set that includes a filter. Infusions should be started initially at a slower rate (0.1 to 0.2 ml/kg over 10 to 20 minutes) observing the patient for evidence of a transfusion reaction (i.e., vomiting, hyperthermia, defecation, hypertension, hypotension, tachycardia, angioedema, etc). The remainder of the infusion can be administered at up to 20 ml/kg/hour.

Polymerized ultrapurified bovine hemoglobin is solution capable of improving both oxygen carrying capacity and colloid oncotic pressure as a result of the oxygen-binding capacity of the free hemoglobin and the high colloidal oncotic pressure of the solution (Creteur, Sibbald, Vincent, 2000). There are reports of hemoglobin-based products being used in non-domestic species to support blood volume (Lichtenberger, 2004). In non-domestic animals these solutions are an attractive option in that they should be associated with minimal risk of immunological reactions, they do not require collection from a donor animal and have a relatively long shelf-life. However, these products have been associated with some adverse myocardial and vascular events (Gibson et al., 2002) and are currently erratically available. No dosing guidelines are available for these products in non-domestic animals.

Specific Cardiovascular Anesthetic Complications

Bradycardia Bradycardia is defined as a heart rate below normal values. There are a variety of normal values depending on species, size, fitness status, etc. In general smaller animals have a higher basal heart rate. In order to define bradycardia in a particular species, it is important to be familiar with normal heart rates in the species of interest. For many species normal heart rates in awake animals are poorly characterized; metabolic scaling formula can be used to estimate heart rates in these species (Abou-Madi, 2006). Birds tend to have higher heart rates than comparatively sized mammals, whereas reptiles tend to have much lower heart rates compared with a similar-sized mammal. Bradycardia is most often caused by relative or absolute elevations in parasympathetic tone (vagal stimulation). This can be the result of abolishing sympathetic tone (e.g., general anesthesia) and increasing relative vagal tone, by directly increasing vagal tone (e.g., opioids) or via reflex increases in vagal tone (e.g., baroreceptor response, oculocardiac reflex). Other causes include hypothermia, electrolyte abnormalities (e.g., hyperkalemia), or cardiac conduction abnormalities (e.g., heart block). Most causes of bradycardia are responsive to anticholinergics such as glycopyrrolate (0.005 to 0.01 mg/kg intravenously [IV] or intramuscularly [IM]) or atropine (0.01 to 0.04 mg/kg IV or IM). However, bradycardia resulting from hypothermia

and hyperkalemia as well as some heart diseases is often poorly responsive to anticholinergic therapy. Atropine causes a fast and more pronounced effect and should be used in severe bradycardia. Both glycopyrrolate and atropine can cause a decrease in heart rate before the expected increase occurs. This reduction in heart rate is normally transient and usually can be corrected by administering an additional dose of an anticholinergic. The decision to treat a low heart rate should be based on an understanding of the underlying cause and the significance of the bradycardia to the patient. Bradycardia can cause decreases in cardiac output and blood pressure, leading to an overall reduction in tissue perfusion; hence, it is probably prudent to treat most bradycardias. However, under some circumstances this may be less desirable, as increased heart rates are associated with increased myocardial work and oxygen consumption that may not be desirable in some patients. Another controversial situation is the use of anticholinergics in conjunction with α -2 agonists. α -2 Agonists cause a reflex bradycardia in response to the hypertension associated with their administration. (This is more pronounced when the drugs are given IV rather than IM.) In this situation the bradycardia is a normal response to the hypertension and there is some evidence that increasing the heart rate with an anticholinergic may increase the incidence of arrhythmias and increases myocardial oxygen consumption secondary to an increase in myocardial work potentially leading to myocardial hypoxia (Sinclair et al., 2003). There is currently no general consensus on the safety of concurrent anticholinergic and α -2 agonist administration (Sinclair, 2003; Lemke, 2004).

Tachycardia Tachycardia is a significant elevation in heart rate above normal. Tachycardia increases myocardial work and oxygen consumption, and can reduce myocardial perfusion. Tachycardia may predispose patients to undesirable cardiac events in those predisposed to myocardial ischemia. Tachycardia is probably most often associated with hypovolemia, inadequate analgesia/anesthesia, drugs (e.g., ketamine, tiletamine), and elevations in sympathetic tone associated with the stress of capture. Treatment is usually directed at identifying and correcting the underlying cause. Rapid fluid administration (10 to 20 ml/kg IV over 15 minutes) can be very effective in reducing elevated heart rates and reestablishing blood volume. The administration of an appropriate analgesic or adjusting the depth of anesthesia may decrease sympathetic responsiveness and reduce elevations in heart rate. It is very uncommon to require pharmacological intervention with β-blockers or calcium channel blockers and use of these drugs without a good understanding of the patient's cardiovascular function and close monitoring is not recommended.

Hypotension In most mammalian species low blood pressure is considered to be a mean BP less than 60 mmHg

and a systolic pressure less than 90 mmHg. In reptiles and birds normal blood pressure is less well characterized; thus, hypotension is more difficult to define. Reductions in blood pressure are most often linked with drugassociated cardiovascular depression (excessive anesthetic depth), hypovolemia, or peripheral vasodilation. Treatment should be aimed at verifying the accuracy of the blood pressure measurement, evaluating the patient for excessive anesthetic depth, correcting bradycardia, and providing fluid support to offset hypovolemia, dehydration, and vasodilation. Occasionally blood pressure values can be erroneous because of cuff misplacement, arrhythmias, or equipment failures. If a low heart rate accompanies hypotension, a dose of an anticholinergic (glycopyrrolate 0.01 mg/kg; atropine 0.02 to 0.04 mg/kg) may be effective for raising blood pressures by increasing heart rate and consequently increasing cardiac output. Anticholinergics will do little to improve blood pressure in patients that have normal or elevated heart rates. Excessive anesthetic depth is a common cause of hypotension in anesthetized patients. Most anesthetics (particularly inhalants) reduce myocardial contractility, cardiac output, and vascular responsiveness (baroreceptor response), cause vasodilation, and diminish sympathetic tone, all leading to reductions in blood pressure. Careful assessment of anesthetic depth is necessary to ensure the patient is at an appropriate plane of anesthesia for the procedure. Lightening the anesthetic depth is generally associated with improvements in cardiac performance and blood pressure. Peri-anesthetic fluid administration can help offset some of the vasodilation and can maximize cardiac function in anesthetized patients. Fluid bolus administration (10 to 20 ml/kg over 15 minutes) is commonly used to rapidly expand intravascular volume and improve cardiac output and blood pressure. Specific fluids types and some indications are discussed in the preceding. Occasionally hypotension fails to correct with the described treatments and a sympathomimetic may be required. Commonly used sympathomimetics in domestic species include dopamine, dobutamine, and ephedrine. The effects of these drugs on blood pressure and cardiovascular performance vary among species and careful monitoring and observation are required to avoid unwanted side effects, such as tachycardia and other arrhythmias. Both dopamine and dobutamine have relatively short elimination halflives and must be given by infusion to sustain their effects. Dopamine is a directly acting, endogenous catecholamine that has unique dose-dependent effects on renal perfusion, cardiac contractility, and peripheral vascular tone. At low doses (1 to 5 µg/kg/minute) dopamine causes renal vasodilation in species possessing renal dopaminergic receptors. At mid-range doses (5 to 10 µg/ kg/minute) dopamine tends to improve cardiac contractility by acting on myocardial β1 receptors. This is associated with improvements in blood pressure. At high doses (greater than 10 µg/kg/minute) the vasoconstrictive

effects of dopamine acting on α1 receptors tends to predominate. This increases blood pressure, but may decrease tissue perfusion to some organs. Dobutamine is a direct-acting synthetic catecholamine with predominantly β 1 effects, but also some β 2 effects (Laste, 2001). Dobutamine tends to predictably increase cardiac output, but may have minimal effects on blood pressure as a result of its β2 vasodilatory effects in some species. However, in equine patients dobutamine tends to predictably increase blood pressure and cardiac output (Young et al., 1998). Ephedrine is a synthetic direct and indirect acting noncatecholamine sympathomimetic. Ephedrine has a longer duration of action compared with dopamine and dobutamine and can be used to support cardiovascular function when an infusion is either not desirable or not possible. Ephedrine acts directly and nonspecifically at both α and β receptors. Ephedrine also causes the endogenous release of norepinephrine. The cardiovascular effects are similar to epinephrine but less intense.

Hypertension Hypertension is an uncommon finding in most patients and rarely requires treatment. However, hypertension is a common side effect of α_2 -agonists. The hypertension is related to the α_1 - and α_2 -agonist activities of these drugs. Increased systemic vascular resistance can lead to a significant decrease in cardiac output and increased myocardial workload (Pypendop, Serteyn, and Verstegen, 1996; Pypendop and Verstegen, 1999). Severe peripheral vasoconstriction also may decrease the oxygen delivery and blood supply to the periphery (muscles, skin). The use of drugs with vasodilating effects to offset vasoconstriction is uncommon and requires careful monitoring and a sound knowledge of their mechanisms of action and effects on the patient.

Arrhythmias Arrhythmias can occur and may be related to underlying diseases of the heart, acid-base abnormalities, hypercarbia, hypoxemia, electrolyte abnormalities, alterations in sympathetic (painful stimuli) and parasympathetic tone, as well as various systemic illnesses. Underlying causes should be investigated and corrected and the arrhythmia should be characterized as atrial or ventricular in origin. Treatment is generally dependent on the significance of the arrhythmia to the patient. Occasional arrhythmias (1 to 2/minute) may not pose any significant problems to most patients; however, if the arrhythmias are frequent (more than four in a row/minute), have abnormal or alternating complexes, or are associated with significant alterations in blood pressure, treatment should be initiated. Lidocaine is the drug of choice for most ventricular arrhythmias, such as ventricular premature contractions (VPCs) and is generally given as a bolus of 1 to 2 mg/kg and can be administered as a CRI of 50 to 100 µg/kg/minute if the arrhythmia persists. Many atrial arrhythmias are associated with alterations in sympathetic and parasympathetic tone and are generally less responsive to lidocaine. Treatment of atrial arrhythmias is often more problematic and depends upon the cause of the arrhythmia. Generally first- and second-degree heart blocks can be successfully treated with an anticholinergic given at standard doses.

Cardiac Arrest Cardiac arrest can occur for many reasons (drugs, underlying cardiovascular disease, electrolyte imbalances, respiratory arrest, hypothermia, and autonomic imbalances). The basic principles of cardiopulmonary resuscitation (CPR) should be followed during any attempt to resuscitate (Hackett, 2001). Time is crucial and ideally all emergency drug doses should be calculated before the start of the procedure (and even drawn up into syringes in high-risk patients) and readily available. The importance of preparedness cannot be overemphasized. An emergency kit should be available containing equipment and drugs suitable for supporting a cardiac arrest, and all members of the staff involved with animal immobilization and anesthesia should be trained in CPR. Organization during an arrest is also extremely important; it is best if a single individual directs the arrest assigning responsibilities to others involved in the CPR. Finally, resuscitation expectations should be realistic. A patient with a critical or terminal illness is unlikely to respond favorably to resuscitation attempts, and if the cause leading to the arrest is irreversible, it may be best to consider the arrest death. Also our ability to perform effective CPR (chest compressions) in many larger patients (greater than 200 kg) is poor to impossible; hence, if an arrest occurs in one of these animals, our expectations should be lowered to reflect the reality of the situation. However, if the arrest is primarily respiratory in origin, patients often respond favorably to supplemental respirations and sympathomimetic support. It is common in domestic animals to discontinue all anesthetics and occasionally even reverse some of the drugs (α -2 agonists). For nondomestic species these recommendations probably also apply, but the possibility of unexpected arousal should be considered if all anesthetic and immobilizing drugs are discontinued or reversed. This situation could lead to serious personnel safety issues, particularly when large and potentially dangerous species are being anesthetized. Supplemental anesthetic drugs (e.g., inhalant anesthesia, ketamine, or propofol) should be readily available and immediate retreat to a safe position should be available. In general the ABCDs of CPR should be followed in patients who have arrested—airway, breathing, circulation (cardiac compressions), and drugs. An airway should be secured if not already available. An appropriate-size endotracheal tube allows for the administration of manual ventilations. However, if an endotracheal tube is unavailable, any other means should be used to provide supplemental oxygen (e.g., stomach tube or insufflation tube passed into the trachea). Manual respirations can be given using either

the rebreathing bag of an anesthetic machine or an Ambu-bag attached to an endotracheal tube. In birds the air sacs are a suitable option for providing supplemental oxygen and manual respirations. Cardiac compressions can be applied directly to the heart in small animals and those with dorsoventrally flattened chest cavities (primates and monkeys). Manual respirations are normally interspersed between chest compressions rather than simultaneously with chest compressions (Hackett, 2001). In many larger species with deep chest configurations, chest compressions are applied to the chest cavity and the force from compressions is transferred across the chest tissues (lungs), leading to compression of the heart. This is referred to as the thoracic pump technique. The heart is not compressed directly owing to the width across the chest and the size of the heart. In these animals it is best to administer breaths with chest compressions in order to limit the loss of force from the chest compressions. By applying slight pressure on the rebreathing bag or Ambu-bag simultaneously with each chest compression, the efficacy of chest compressions administered between respirations may be improved by limiting the amount of air from escaping the chest cavity. Chest compressions should be given at a rate similar or greater than normal heart rate for the given species (i.e., 60 to 300 compressions per minute). In general, chest compressions in smaller patients are much more rapid than those for larger species. Recommended chest compression-ventilation ratios range from 15:1 to 3:1 (ILCOR, 2006). In general there is evidence in human CPR suggesting that greater emphasis should be placed on providing effective chest compressions rather than ventilation (Hazinski et al., 2005). Chest compressions are most effective when applied by pushing hard and fast and by minimizing interruptions. It is also important to evaluate the effectiveness of compressions by assessing blood flow; this is best done by evaluating the pulse quality in a major artery (i.e., femoral artery). If no pulses are detectable with compressions, the technique of applying chest compressions should be altered slightly. Blood flow can also be assessed using a Doppler placed over an artery or even the eye. If a capnography device is available it can be used as an indirect indicator of the quality of blood flow and to evaluate the resuscitation (Callaham and Barton, 1990). An ECG can be used to assess heart rate and rhythm. The cardiovascular support drugs are best given intravenously; however, they can be administered intra-tracheally. If they are given via the endotracheal tube, the doses are normally doubled and they are diluted in a small volume of saline to increase the volume. The most commonly used cardiovascular support drugs during CPR are atropine, epinephrine, and lidocaine. In general epinephrine is administered to patients who do not respond to basic CPR (manual ventilation and chest compressions) within 30 to 60 seconds. Epinephrine stimulates the myocardium and

causes vasoconstriction (Brown, Martin, and Pepe, 1992; Van Pelt and Wingfield, 1992). The vasoconstriction associated with epinephrine centralizes blood flow and is believed to be its primary beneficial effect during CPR. Other vasoconstriction drugs with fewer myocardial side effects, such as phenylephrine, methoxamine, and vasopressin also have been evaluated, but so far none has been shown to be more effective than epinephrine. Atropine is also frequently used early in an arrest to eliminate vagal effects that may have contributed to the arrest or may impede resuscitation attempts. Lidocaine is used to manage ventricular arrhythmias and stabilize myocardial membranes. Lidocaine does have myocardial depressant effects in some species; thus, it should only be used when indicated (Pypendop and Illkiw, 2005).

RESPIRATORY SUPPORT

General

Most anesthetics cause mild to moderate respiratory depressant effects, which can lead to changes in respiratory rate and/or pattern and a diminished or altered response to O₂ and CO₂. The depth of anesthesia is directly associated with alveolar ventilation. As anesthetic depth increases the sensitivity of the respiratory center to CO₂ decreases, leading to a reduction in alveolar ventilation and an increase in CO₂ retention (hypercarbia). In addition, the ventilatory response to hypoxia is blunted. These alterations make the patient more susceptible to complications associated with both hypercarbia and hypoxia. Body position and underlying respiratory disease (upper airway and pulmonary) can also play important roles in the maintenance of alveolar ventilation and oxygen exchange. Careful monitoring of the respiratory system helps prevent and manage some of these complications. The capnograph is one of the most useful non-invasive monitors for assessing the quality of alveolar ventilation. Capnography measures the amount of CO₂ in inspired and expired (end-tidal) gases. In patients with normal respiratory function, capnography can be used as an estimate of arterial CO₂ levels. However, the accuracy of capnography can be affected by alterations in respiratory function (e.g., dead space ventilation, rapid shallow breathing), patient factors (e.g., size), equipment (e.g., non-rebreathing versus rebreathing systems), and the type of capnograph (e.g., main stream or side stream). Observation of respiratory rate alone may be misleading; tidal volume should be evaluated also, because deeper breaths are associated with improved ventilation (greater alveolar ventilation) compared with shallow breaths. Oxygenation (hemoglobin saturation) is best assessed using a pulse oximeter. Unfortunately, skin pigmentation, arrhythmias, vasoconstriction (e.g., α -2 agonist, hypothermia), and abnormal hemoglobin species (e.g., methemoglobin) can all affect the ability of pulse oximeters to accurately

assess hemoglobin saturation. Arterial blood gas analysis is the most accurate method of assessing respiratory function, but is not practical in some situations because of the impracticality and cost of the majority of instrumentation. However, portable hand-held analyzers are available and can be used easily in remote situations.

Routine administration of oxygen, even in field and remote situations, can reduce the incidence of hypoxia (Read, Caulkett, and Symington, 2001). Cyanosis is a late sign of hypoxia; thus, mucous membrane color should not be considered a sensitive indicator of oxygenation (Daley, Norman, and Colmenares, 1991). Supplemental oxygen should be administered as close to the site of gas exchange (the alveoli) as possible. An endotracheal tube is probably the most desirable method for providing supplemental oxygen. In addition to oxygen supplementation, the endotracheal tube provides a means for delivering ventilatory support and protects the airway from inadvertent aspiration. An anesthetic system with a rebreathing bag or an Ambubag can be used to ventilate the intubated patient.

Specific Respiratory Complications

Hypoventilation/Hypercarbia Hypoventilation causes carbon dioxide to be retained, leading to hypercarbia. Hypoventilation is best evaluated by assessing the CO₂ level in the blood. This can be done directly using a blood gas analyzer or indirectly using a capnometer or capnograph that measures end-tidal CO₂ (ETCO₂). As mentioned, the evaluation of respiratory rate alone is not always a sensitive indicator of hypoventilation. For example, a rapid shallow respiratory pattern is generally associated with limited alveolar ventilation; hence, hypoventilation may be present despite the elevated respiratory rate. Hypoventilation is best described as a respiratory pattern resulting in an accumulation of carbon dioxide (hypercarbia). This is most often a result of inadequate alveolar ventilation. The evaluation of both rate and depth of respiration are required to assess ventilation. If hypoventilation is suspected or confirmed (hypercarbia), treatment should begin by identifying the underlying cause of hypoventilation and if possible it should be corrected. It is common to have some hypoventilation associated with anesthetics and some anesthetic adjuncts. The inhalant anesthetics are associated with dose-dependent hypoventilation. The opioids, in particular the potent opioids (e.g., carfentanil, etorphine), also can cause some mild hypoventilation when used alone, but this effect can become pronounced when they are combined with anesthetics and sedatives. If hypoventilation cannot be managed by adjusting anesthetic depth, intubation of the animal and intermittent positive pressure ventilation (IPPV) via an anesthetic breathing system or an Ambu-bag is advisable. Appropriate manual ventilation of the patient will correct hypoventilation and hypercarbia. General guidelines for manual or automated ventilation using a

ventilator are: tidal volume 10 to 20 ml/kg and a rate appropriate for the species, which may range from 2 to 60 bpm. In most circumstance the goal for an ETCO $_2$ or blood CO $_2$ should be 35 to 45 mmHg for most species. Hyperventilation should be avoided to limit the period of apnea once ventilation is discontinued.

Apnea and Respiratory Arrest Apnea and respiratory arrest are not uncommon in some species and require immediate intervention. Recognizing a change of breathing pattern and rate early with monitoring equipment such as a capnograph may give advanced warning of this complication. Treatment of respiratory arrest is similar to that of hypoventilation but requires more prompt intervention. The easiest method of treatment is to assume respiratory control for the patient. This requires intubation of the patient with an endotracheal tube. Airway patency should be assessed also to rule out the possibility of a correctable airway obstruction. Assessment of the patient's depth of anesthesia should be performed and corrected if necessary. Reversal drugs may reverse respiratory arrest, but should only be given if their use will not put the patient or personnel at additional risk of injury (Moresco et al., 2001). If intubation is not an option, patency of the airway should be confirmed and manual chest compressions should be started. Respiratory arrest can lead quickly to cardiovascular arrest under some circumstances. The animal can be repositioned to improve airflow, and reversal agents may need to be employed if the situation allows. Partial reversal of the opioid not only may improve respiration, but can also lead to a reduction in the plane of anesthesia and the loss of analgesia. Respirations can sometimes be initiated by stimulating the acupuncture point (Jen Chung) on the phylum of the nose with a needle (Davies, Janse, and Reynolds, 1984; Skarda, 1999). The placement of the needle may initiate a breath; for additional stimulation, the needle can be gently twisted in place. Other techniques used by the authors to stimulate respirations include twisting the ear, pushing on the chest, and pinching the rectal anus. The use of doxapram is still controversial when used in a hypoxic animal. Doxapram works by stimulating the central nervous system (CNS), which increases respiratory drive while it diminishes cerebral blood flow (Roll and Horsch, 2004). In an already hypoxic patient this may worsen CNS hypoxia, leading to further cell injury and death. However, this effect has not been clearly demonstrated in the clinical environment. Doxapram is probably best used in patients known to be normoxic (SpO₂ greater than 90%).

Airway Obstruction Airway obstruction is a complication that can lead to hypoxia and/or hypercarbia. Obstruction can occur as a result of soft palate displacement; inadequate positioning of the head or neck; or occlusion caused by fluid, mucous, regurgitation

content, or saliva in the laryngeal, nasal, tracheal or bronchial area. Endotracheal tubes can help minimize the risks of obstruction by circumventing the upper airway. However, small endotracheal tubes are susceptible to developing obstruction as a result of mucous plugs; thus, small patients, those with very viscous mucous, and those undergoing prolonged procedures may be at greater risk. Suction of the endotracheal tube and laryngeal area can be done to minimize the risks associated with airway obstructions. Other causes of obstruction may be equipment-related, such as failure to open a closed "pop-off" valve or unintentional kinking of the endotracheal tube or breathing circuit. Patency of the breathing system can be assessed easily in intubated patients by administering a manual breath and listening for lung sounds on both sides of the chest. This can be used to rule out one lung intubation in species with an early tracheal bifurcation. Inspiration should not be associated with excessive pressure, and expiration should occur easily and completely.

Hyperventilation Hyperventilation can occur with animals in a light plane of anesthesia or in those with an elevated body temperature. Hyperventilation may occur in hypoxic and hypercarbic patients as well. Hypoxia can be rapidly life threatening and should be ruled out as quickly as possible. Hypercarbia causing hyperventilation is most often associated with equipment failure that prevents the normal removal of CO₂ from the breathing system (i.e., exhausted soda lyme or an insufficient fresh gas flow using a non-rebreathing system). Panting may be associated with hyperthermia and normally results in a rapid shallow breathing pattern with less efficient gas exchange (alveolar ventilation). This respiratory pattern is also associated with decreased uptake of inhalant anesthetics and may cause a patient to appear to be in a light plane of anesthesia despite adequate or high vaporizer settings. Controlling ventilation using an automated ventilator or manual ventilation may be beneficial for improving the control of anesthetic depth. Careful attention to anesthetic depth is important when instituting controlled ventilation. Controlled ventilation generally improves the delivery of anesthetic gases to the patient, and the depth of anesthesia can be expected to deepen. If the panting is associated with hyperthermia, measures to cool the patient (e.g., ice, alcohol spray, shades) should be instituted.

Hypoxemia Hypoxemia (PaO_2 less than 60 mmHg, SpO_2 less than 90%) is a common complication associated with immobilization and anesthesia, particularly in larger recumbent animals and those breathing "room" air (21% oxygen). Several situations can contribute to the development of hypoxemia: low inspired oxygen, hypoventilation, ventilation/perfusion (V/Q) mismatch, shunts (pulmonary and cardiovascular), or diffusion impairments (respiratory disease).

Low inspired oxygen may contribute to hypoxia in animals anesthetized at elevation. For example, the inspired oxygen at sea level (760 mmHg) is approximately 159 mmHg, although it can be markedly reduced at higher altitude (i.e., at Denver, CO, the local barometric pressure is 550 mmHg and the inspired oxygen is approximately 115 mmHg). Oxygen supplementation can be used to overcome the effects of moderate elevation differences.

Hypoventilation commonly occurs secondary to many anesthetic drugs and adjuncts and may contribute to hypoxemia by limiting the amount of oxygen delivered to the alveoli and increasing the amount of carbon dioxide occupying the alveoli, leaving less space for oxygen. Ultimately treatment should be aimed at identifying and treating the cause of hypoventilation; however, supplemental oxygen can be used to reduce the effects of hypoventilation on oxygenation.

Ventilation-perfusion mismatch is undoubtedly the most common cause of hypoxemia in anesthetized and immobilized animals. In the normal awake animal there are intrinsic compensatory mechanisms in the lung that optimize the matching of ventilation and perfusion, maximizing the efficiency of gas exchange. In recumbent animals and those given anesthetic drugs, these compensatory mechanisms are altered or blunted and gas exchange becomes much less effective. The factors responsible for these alterations are complex but include anatomical features such as shape of the diaphragm and relative volume and structure of abdominal contents (rumen, fetus, etc.), patient positioning, and direct drug effects. Proper patient positioning may help improve V/Q matching during immobilization and anesthesia. Patients should be positioned to limit abdominal pressure on the diaphragm and if possible in lateral rather than dorsal recumbency. Impeding chest movement by leaning or resting equipment on the chest should be avoided, as this exacerbates V/Q mismatch and predisposes the patient to ventilatory compromise. Ropes and ties for restraint can impede chest excursions also, and this possibility should be considered when used. Oxygen supplementation can be used to help limit the effects of V/Q mismatch on oxygenation. Intravascular and intrapulmonary right-to-left shunts bypass the gas exchange surfaces of the lung and can cause profound hypoxemia that is unresponsive to oxygen supplementation. Extreme alterations in V/Q matching (i.e., no ventilation with perfusion, atelectatic lung) behave functionally as a shunt. The effects of atelectasis can be limited by intermittently "sighing" the animal, opening up some of the atelectatic lung.

Diffusion barriers limit oxygen transport to the blood by limiting diffusion across the alveoli. Diffusion impairments are most often associated with diseased lungs (pneumonia or edema). Diffusion impairment hypoxemia can be offset by supplementing the patient with oxygen. Oxygen supplementation increases the

oxygen concentration gradient across the alveoli:capillary improving oxygen diffusion.

In general, supplemental oxygen is a valuable method for improving oxygenation and limiting hypoxemia. Oxygen supplementation can be accomplished easily (Manning, 2002), and many of these techniques can be adapted easily for use in field situations. Most animals at rest breathe through their nose, and oxygen can be supplemented by advancing a small tube into the nasopharyngeal area. Oxygen can be supplied from various sized oxygen tanks fitted with a regulator and flow meter. Several inexpensive models designed for human oxygen therapy are available. These regulators have various flow ranges (1 to 50 L/minute) and some have high flow fittings suitable for use with demand valve systems. Demand valves can be used to deliver a breath should it be required and can be used to improve oxygenation (Riebold, Evans, and Robinson, 1980; Heard, Jacobson, and Brock, 1986; Johnson, Adam, and Taylor, 1994). The flow rates associated with use of demand valves can be very high (40 to 275 L/minute) and should be used with caution in smaller patients (less than 100 kg). Oxygen tanks come in various sizes, but the most practical for field use is an E type cylinder that contains 660 L of compressed oxygen.

 α -2 Agonists are potent and reliable sedatives and analgesics commonly used to facilitate handling and anesthesia of veterinary species. Although these drugs are highly effective, predictable, and reversible, they are not without side effects. In most species the α -2 agonists appear to have minimal respiratory effects. However, their use in ruminants (e.g., cervidae, ovidae) is commonly associated with profound hypoxemia (Moresco et al., 2001; Read, Caulkett, and Symington, 2001; Kaestner, 2006). The cause of hypoxemia is likely related to a combination of factors, including the V/Q mismatch associated with recumbency, but at least in sheep they also cause marked pulmonary edema and hemorrhage that appears to resolve spontaneously with cessation of the drug's effects (Kaestner, 2006). Hypoxemia associated with the use of α -2 agonists in ruminants can be limited by using oxygen insufflation (Read, Caulkett, and Symington, 2001).

Pneumothorax Pneumothorax is a potential complication encountered following dart misplacement into the thoracic wall or cavity. In animals with a heavy hair coat, dart misplacement may not always be readily identified during initial immobilization. If this does occur and the animal fails to become immobilized, another dart may be necessary to complete the immobilization. Pneumothorax is potentially a rapidly life-threatening incident and its identification and treatment should not be delayed. Upon immobilization the animal immediately should be given supplemental oxygen and the chest should be auscultated for lung sounds. A pulse oximeter can be used to assess hemoglobin saturation.

If lung sounds cannot be auscultated and there are additional typical signs of a pneumothorax (e.g., rapid respirations with minimal chest excursions, tympany associated with percussion, barrel-shaped chest) it is likely that a significant pneumothorax is present. An appropriate-sized needle attached to a three-way stopcock (preferably with an extension set) and a large syringe can be used to remove air from the chest cavity. The needle should be introduced slowly into the highest point of the chest cavity with an assistant applying gentle back-pressure on the syringe. The needle should be advanced to a point at which air can be removed. Removal of air under these circumstances generally results in dramatic improvements in respiratory function. If a pneumothorax is not present, the dart should be carefully removed and the hole in the chest wall closed. Once the chest wall is closed the chest should be re-auscultated for lung sounds and the respiratory pattern and hemoglobin saturation should be evaluated. It is not uncommon for a small amount of air to remain even after thorough thoracocentesis and this is generally well tolerated by most healthy animals. Chest tube placement and closed suction systems may be considered, but generally are not feasible in nondomestic species.

CONCLUSIONS

In general, most cardiopulmonary complications can be best managed with an appropriate understanding or cardiopulmonary physiology and pharmacology. In addition, careful monitoring can help in the recognition and treatment of many complications. The importance of proper monitoring and patient evaluation cannot be overemphasized.

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Stress

Jon M. Arnemo and Nigel Caulkett

INTRODUCTION

In biology and medicine, *stress* refers to the generalized, non-specific response of the body to any factor that overwhelms, or threatens to overwhelm, its compensatory abilities to maintain homeostasis. The agent or stimulus inducing this response is known as a *stressor*. Stress is a natural part of an animal's daily life and is not inherently bad. In fact, stressors may evoke responses that are beneficial for the animal's ability to survive. Such stress is known as *eustress*, or "good stress." In contrast, stimuli such as pursuit, restraint, pain, and anesthesia are capable of inducing harmful responses and pathological changes. When the stress response truly threatens the animal's well-being, the individual experiences *distress*, or "bad stress."

This chapter deals with medical aspects of acute stress during capture and chemical immobilization of free-ranging wild animals. In captivity, individual animals are often accustomed to handling and the presence of humans and severe distress during restraint or anesthesia is less likely to develop.

STRESS PHYSIOLOGY

The prevention, diagnosis, and treatment of distress in animals require a basic understanding of its neural and endocrine responses. For a more comprehensive coverage of stress physiology, readers are referred to current textbooks (Moberg and Mench, 2000; Reece, 2004; Sherwood, 2004; Ganong, 2005; Wiedmaier, Raff, and Strang, 2005; Guyton and Hall, 2006).

Stress can be induced by a number of noxious or potentially noxious stimuli, including physical (trauma, surgery, intense heat or cold); chemical (reduced oxygen supply, acid-base imbalance, anesthetic drugs); physiological (heavy exercise, hemorrhage, shock, pain, infection); and emotional (anxiety, fear) stressors. Although different stressors may produce some specific responses

characteristic of that stressor, all stressors also produce a similar non-specific, generalized response regardless of the type. When a stressor is recognized, both neural and hormonal responses are activated to cope with the emergency. All the individual responses to stress are either directly or indirectly influenced by the hypothalamus. The hypothalamus receives input concerning stressors from virtually all areas of the brain and from many receptors throughout the body. In response, the hypothalamus activates the sympathetic nervous system and the hypothalamus-pituitary-adrenal axis.

Activation of the Sympathetic Nervous System

The major neural response to acute stress is a generalized and immediate activation of the sympathetic nervous system, known as the fight-flight response because an animal in this state decides almost instantly whether to stand and fight or run. In either event, the sympathetic alarm reaction makes the animal's subsequent activities more vigorous. One of the most striking characteristics of the sympathetic nervous system is the rapidity and intensity of its response to a stressor. For instance, within 3 to 5 seconds the heart rate can be doubled, and within 10 to 15 seconds the arterial blood pressure can be increased to twice normal.

A massive outpouring of catecholamines (epinephrine and norepinephrine) occurs from the adrenal medulla. Catecholamine release induces a wide range of physiological effects that enhance the animal's ability to cope with an emergent situation. These acute adaptations include the following: increased heart rate, arterial blood pressure, and cardiac output (secondary to increased cardiac contractility and heart rate). Blood flow to skeletal and cardiac muscles increases because of vasodilatation by as much as 400% from the resting state. Blood flow decreases because of vasoconstriction by as much as 90% to visceral organs, such as the gastrointestinal tract and kidneys. Splenic contraction can increase the packed cell volume by as much as 50%.

Increased platelet aggregation occurs, which enhances coagulation. Catecholamines induce decreased motility and contraction of sphincters in the gastrointestinal tract and relaxation of the urinary bladder with contraction of its sphincter. Cellular metabolism throughout the body can be increased by up to 100% from resting. Inhibition of insulin secretion and stimulation of glucagon secretion increases blood glucose concentration because of glycogenolysis in the liver and muscles. During anaerobic metabolism lactic acid is released from the muscles and converted to glucose in the liver. Ventilation increases (via central stimulation), which is accompanied by bronchiolar dilation. Ocular effects include dilatation of the pupil and adjustment of the eyes for distant vision. Central effects include increased alertness and mental activity. Catecholamine release strengthens the sympathetic responses and reaches places not innervated by the sympathetic nervous system. The sum of all these effects permits an animal to perform more strenuous exercise than would otherwise be possible.

Catecholamine secretion by the adrenal medulla is controlled entirely by sympathetic input to the gland. In fact, the adrenal medulla is composed of modified postganglionic sympathetic neurons. When the sympathetic system is activated during stress, it simultaneously triggers an immediate surge of adrenomedullary catecholamine release, flooding the circulation with up to 300 times the normal concentration of catecholamines. Although a number of different stressors have been shown to influence adrenal catecholamine secretion, they all act by increasing preganglionic sympathetic impulses to the adrenal medulla. The amount of catecholamines released depends on the type and intensity of the stressful stimulus. The circulating catecholamines have almost the same effects on the different organs as those caused by direct sympathetic nervous stimulation. However, the effects last 5 to 10 times as long because the circulating catecholamines are removed from the blood slowly.

The ratio of epinephrine to norepinephrine secreted by the adrenal medulla varies considerably among species and with age. Epinephrine usually predominates over norepinephrine in adult mammals. In whales and some avian species, however, about 80% of the catecholamine output from the adrenal medulla is norepinephrine. In the fetus and newborn animal, norepinephrine is also the predominant catecholamine. Epinephrine and norepinephrine have differing affinities for the alpha and beta adrenoceptors and their subtypes, which varies among tissue types and animal species.

Activation of the Hypothalamic-Pituitary-Adrenal Axis

The predominant hormonal response during both acute and chronic stress is activation of the hypothalamicpituitary-adrenal axis. Neural input to the hypothalamus, from the central nervous system, in response to a stressor induces secretion of the corticotropin-releasing hormone (CRH). CRH is carried by the hypothalamic-pituitary portal vessels to the anterior pituitary and stimulates adrenocorticotropic hormone (ACTH) release. ACTH circulates to the adrenal cortex and stimulates release of glucocorticoid hormones (cortisol and corticosterone). During acute stress, secretion of glucocorticoids may increase as much as 20-fold within 5 to 20 minutes after a stressor has been recognized. Birds and rodents secrete corticosterone almost exclusively. Canids secrete approximately equal amounts of both glucocorticoids. Felids, ungulates, and primates secrete predominantly cortisol.

Glucocorticoid secretion by the adrenal cortex is regulated by a negative-feedback system. Glucocorticoids have an inhibitory effect on CRH and ACTH secretion. In a normal situation, the negative feedback system for glucocorticoids maintains a relatively constant level of glucocorticoid. This constant secretion is punctuated by alternating bursts of low-level secretion separated by periods of little or no secretion. The amount of glucocorticoids secreted with each burst is relatively constant from one secretory episode to the next; however, the total amount of glucocorticoids secreted during a given period of time can be changed by altering the frequency of secretory bursts. One burst adds to the previous burst, increasing the blood concentration of glucocorticoids beyond that achieved by a single burst. In some species, glucocorticoid secretion follows a circadian rhythm. This rhythm is intrinsic to the hypothalamic-pituitary control system and can be related primarily to the sleepwake cycle or to seasonal variation possibly related to changes in daylight length. These variations are small compared with the dramatic increase in glucocorticoid secretion during acute stress. The magnitude of increase in blood glucocorticoid concentration is generally proportional to the intensity of the stressful stimulation. A greater increase in cortisol levels is evoked in response to severe stress than to mild stress.

It has become clear that the secretion of ACTH, and glucocorticoids, is stimulated by several hormones in addition to hypothalamic CRH. These include vasopressin, released from its stores in the posterior pituitary gland, and catecholamines. Several cytokines, including interleukin 1, stimulate ACTH secretion and provide a means for eliciting a classical stress response when the immune system is stimulated.

The major metabolic effect of increased glucocorticoid secretion during stress is to mobilize fuel. Plasma concentrations of amino acids increase because of catabolism of body protein stores in muscle. Glycerol and fatty acids are increased by triacylglycerol catabolism in adipose tissue. Blood glucose is increased by gluconeogenesis from amino acids, glycerol, and lactate and by inhibition of glucose uptake and oxidation by many body cells. These effects are ideally suited to meet stressful situations. An animal faced with a life-threatening

situation must forgo eating, and these metabolic changes are essential to survive fasting. The amino acids liberated by catabolism of labile body protein stores also constitute a potential source of amino acids for tissue repair should injury occur; thus, an increased pool of glucose, amino acids, and fatty acids is available for use as needed. Glucocorticoids also enhance vascular reactivity, i.e., increased ability to maintain vasoconstriction in response to catecholamines and other stimuli. During stress and prolonged activation of the hypothalamic-pituitary-adrenal axis, glucocorticoids may have antiinflammatory effects and may inhibit specific immune responses.

In addition to its effect on cortisol secretion, ACTH may play a direct role in resisting stress. ACTH is one of several peptides that facilitate learning and behavior. It is possible that an increase in ACTH during stress might condition the body to cope with similar stressors in the future by facilitating the learning of appropriate behavioral responses. ACTH is not released alone from its anterior pituitary storage vesicles. Pruning of the large proopiomelanocortin precursor molecule yields not only ACTH but also β -endorphin and similar compounds. These compounds are co-secreted with ACTH upon stimulation by CRH during stress. It has been hypothesized that β-endorphin, a potent endogenous opioid, may exert a role in mediating analgesia should physical injury be inflicted during stress. It is further speculated that these co-secreted peptides have possible roles in learning, mood alterations, and appetite suppression.

Other Hormonal Changes

In addition to the immediate release of catecholamines and glucocorticoids, with subsequent effects on glucagon and insulin secretion, other hormonal changes occur during acute stress. The renin-angiotensin-aldosterone system is activated as a consequence of a sympathetically induced reduction of blood supply to the kidneys. Vasopressin secretion is also increased during stress. Collectively, these hormones expand the plasma volume by promoting retention of sodium and water. Presumably, the enlarged plasma volume serves as a protective measure to help sustain blood pressure should acute loss of plasma fluid occur through hemorrhage or sweating. Vasopressin and angiotensin also have direct vasopressor effects, which would be of benefit in maintaining an adequate arterial pressure in the event of acute blood loss. Almost every known hormone may be influenced by stress (e.g., prolactin, growth hormone), and thyroid hormones are often increased, whereas the pituitary gonadotropins and the sex steroids are decreased. These changes have no clinically significant effects during brief periods of acute stress.

How to Measure Stress

Invariably, stressors increase the secretion of glucocorticoids (cortisol and/or corticosterone), and the term

stress has come to mean any event that elicits release of these hormones. The stress response is a series of extremely complex and interrelated hormonal and neural events influenced by numerous agents and stimuli, yet blood cortisol levels have been widely used as *the* indicator of stress in both humans and animals. Measurement of blood concentrations of glucocorticoids also has been used to assess capture stress in freeranging wild animals (e.g., Franzmann, Flynn, Arneson, 1975; Morton et al., 1995).

Fear, heavy exercise, starvation, infection, anesthesia, and pain are stressors that might elicit identical activation of the HPA-axis. Animals are known to secrete similar amounts of glucocorticoids during exercise, restraint, and mating. Studies in reindeer (Rangifer tarandus tarandus) and caribou (R. t. caribou) show some of the inherent difficulties of using blood cortisol levels to assess stress. The baseline (resting) level of cortisol in reindeer is probably below 30 nmol/L (Sire, Blom, and Sjaastad, 1995). In captive, semi-domestic reindeer that were used to handling, plasma levels of cortisol increased to 150 to 180 nmol/L after light restraint and blood sampling by jugular venipuncture (Sire, Blom, and Sjaastad, 1995; Arnemo & Ranheim, 1999). In semidomestic reindeer kept in a corral and captured and restrained by means of a lariat, the mean serum cortisol level in 10 animals was 441 (range 249 to 596) nmol/L (Arnemo, unpublished data). An adult semi-domestic female reindeer that was brought into captivity because of severe emaciation, had a serum cortisol level of 465 nmol/L 3 hours before it died (Arnemo, unpublished data). Emotional stress in semi-domestic reindeer exposed to low levels of physical activity may have blood cortisol levels ranging from 100 to 200 nmol/L. In addition to handling, physical restraint, and body condition, anesthetic drugs and method of drug administration influence the blood level of cortisol. In five semi-domestic reindeer kept in a research facility, the mean serum cortisol concentration was 350 nmol/L 30 minutes after administration of medetomidine, two times the pre-treatment level (Arnemo & Ranheim, 1999). At 60 minutes post-medetomidine, when sedation was reversed by atipamezole, a decline in serum cortisol had started, but pre-treatment levels were not reached until 4 hours after administration of medetomidine. In captive, semi-domestic reindeer immobilized with medetomidine-ketamine (Ryeng, Arnemo, and Larsen, 2001; Ryeng et al., 2001), cortisol levels increased two- to threefold during a 30-minute monitoring period, reaching mean levels of 220 to 300 nmol/L, in three different experiments using different doses and methods of drug administration (Ryeng, personal communication). The increase started between 10 and 30 minutes after drug administration. After hand syringe injection, a higher increment was seen when the doses were increased by 50% and a further increase was seen when the drugs were administered by dart

syringe injection. In free-ranging reindeer, the mean serum cortisol level was 303 (range 167 to 477) nmol/L in 27 adult animals immobilized with medetomidine-ketamine from a helicopter (Arnemo, unpublished data). In caribou captured by net gun from a helicopter, Oakley et al. (2004) found that the mean serum cortisol level in animals sedated with medetomidine (n = 18) was not significantly different from untreated controls (n = 18): 182 versus 192 nmol/L.

The effects of anesthetic drugs on cortisol secretion are very complex. α -2 Adrenoceptor agonists such as xylazine and detomidine are known to reduce the stress response, evidenced by decreased serum cortisol. Medetomidine, a more potent α -2 adrenoceptor agent increases the secretion of cortisol in species such as reindeer and moose (*Alces alces*), while a reduction in cortisol secretion is seen in brown bears (*Ursus arctos*) and wolves (*Canis lupus*) (Arnemo, unpublished data). The effect of medetomidine on cortisol secretion may be age dependent, as increased secretion is found in adult dairy cattle but not calves (Ranheim et al., 2000). Very little is known about specific effects on glucocorticoid secretion of other sedative or anesthetic agents in wild animals.

Obviously, measurement of cortisol alone cannot be used to differentiate between non-threatening stress and distress, as cortisol levels are influenced by many factors, including: the baseline ("normal") level of the species; physiological condition of the individual animal; effect of stressors (e.g., fear, pursuit, restraint, capture method, and pain); pathological conditions; type of drug; and method of drug administration. Many other parameters (e.g., glucose) are influenced by stressors and drugs. Assessment of stress during capture and anesthesia should be based on clinical examination, monitoring of vital signs, and measurement of selected blood constituents. This requires the establishment of reference ranges for baseline, safe, and critical levels of a wide range of physiological parameters in each target species.



Figure 8.1. Open-mouth breathing is a sign of hyperthermia in reindeer.

PHYSIOLOGICAL EFFECTS OF CAPTURE

Fear, pursuit, physical restraint, and/or chemical immobilization of wild animals elicit an acute stress response that may compromise the physiological homeostasis of an animal and cause distress. The capture event as well as the immobilizing drugs influences physiological parameters and homeostasis in the animal. Muscular activity associated with excitement, pursuit, and resistance to handling result in lactic acid buildup and an increase in body temperature. Increasing lactic acid levels lead to a drop in blood pH with subsequent acidosis. Immobilizing drugs interfere with normal respiratory function and thermoregulation, which can lead to respiratory depression, acidosis, hypoxemia, and hyperthermia. Oxygenation and ventilation are closely related to, and affected by, acid-base balance and electrolyte concentrations. Minute changes in body temperature, respiratory pattern, and metabolic demands can alter this balance, resulting in neurological or myocardial dysfunction, multi-organ failure, capture myopathy, or acute mortality (Spraker, 1993; Williams and Thorne, 1996).

MONITORING, PREVENTION, SUPPORTIVE CARE, AND TREATMENT OF STRESS

Health assessment of free-ranging wild animals is not possible prior to capture and the risk status of the patient cannot be determined. Even with captive wildlife access to the patient, pre-capture physical examination or laboratory work is not possible without restraint. We generally assume that a stress response has been elicited in all patients and that some level of distress will typically develop. Not surprisingly, capture- and anesthetic-related mortalities in wild animals are usually more frequent than in domestic species (Arnemo et al., 2006).

Protocols for anesthesia, monitoring, supportive care, and stress reduction should be developed for each target species (Arnemo et al., 2006). Potential stressors include fear, pain, hyperthermia, hypothermia, hypoxemia, and respiratory and cardiovascular depression. The most important aspect of distress prevention is to minimize the duration of pursuit, restraint, and anesthesia. Treatment of specific disorders such as hyperthermia and hypoxemia must be instituted, but in the case of acute distress immediate reversal of immobilization and release of the animal should be considered. Epinephrine, atropine, doxapram, lidocaine, and reversal agents always should be carried. Fluids should be available for the treatment of shock, acid-base imbalance, and hypothermia or hyperthermia. Equipment and drugs to treat injuries, infections, and pain should be available. Administration of long-acting tranquilizers is indicated to prevent distress in animals that are being translocated (Ebedes, 1993; Read, Caulkett, and McCallister, 2000; Read and McCorkell, 2002). In field situations it is often difficult to carry all but the most necessary pieces of equipment.

Fortunately there are compact and portable monitors available that are suitable for field use.

Fear is a potent stressor; therefore, following capture a blindfold and earplugs should be used to decrease visual and auditory stimulation. Captured animals should be positioned to ensure optimum ventilation. Vital signs must be monitored frequently. Painful procedures such as tooth extraction or biopsies should be performed soon after induction when the animal is in the deepest plane of anesthesia. Pain is a potent stressor, and provision of appropriate analgesia is important if painful procedures are carried out.

Hypoxemia is a common complication of wildlife anesthesia. Major causative factors include: respiratory depression from immobilizing agents, particularly potent opioids, and ventilation/perfusion mismatching from α₂adrenergic agonists and other causes. Airway obstruction is another common cause, particularly during induction. Immediately after initial contact steps must be taken to ensure a patent airway. The animal should be monitored for hypoxemia continuously with a pulse oximeter. A multi-site sensor applied to the tongue generally provides a good signal. Normal hemoglobin saturation should be 95% to 98%; below 85% is considered hypoxemic. If a pulse oximeter is not available the mucous membranes should be monitored every 5 minutes for cyanosis. Severe hypoxemia is a profound stressor and animals are often tachycardic. Tachycardia, followed by severe bradycardia (heart rate less than 30 beats per minute) is often a warning sign that hypoxemia is very severe and the heart may fail. Supplemental inspired oxygen should be administered in hypoxemic animals. Often nasal insufflation of oxygen is adequate to treat hypoxemia (Read, Caulkett, and Symington, 2001; Read, 2003; Paterson et al., 2006).

A nasal catheter can be used in most animals. The catheter should be threaded as far as the medial canthus of the eye. The flow rate should be adjusted to maintain a saturation greater than 95%. If hypoxemia is severe it can result in vasodilation and death from asystole. Hypoxemia in the face of hyperthermia can rapidly result in tissue hypoxia. This can increase the risk of capture myopathy or result in acute mortality. The best treatment for hypoventilation is intubation and positive pressure ventilation with supplemental inspired oxygen. This can be difficult in field situations. Partial reversal of opioids has been used successfully to treat respiratory depression (Moresco et al., 2001). Hypoxemia resulting from hypoventilation also responds to supplemental inspired oxygen, even though PaCO2 will remain elevated (Schumacher, Citino, and Dawson, 1997; Paterson et al., 2006). Less common causes of hypoxemia include aspiration of stomach contents and pneumothorax.

Heart rate and pulse quality should be monitored every 5 minutes. Equipment is available to measure direct or indirect blood pressure and echocardiogram in the field. This equipment can be valuable in determining trends in heart rate or blood pressure.



Figure 8.2 Nasal insufflation of oxygen in a hypoxemic muskoxen.

Rectal temperature should be monitored every 5 to 10 minutes. Many species are prone to hyperthermia. Causative factors include: high ambient temperatures, excessive muscular exertion from prolonged pursuit, and interference with normal thermoregulatory mechanisms by anesthetic drugs. Symptoms include: measured hyperthermia, rapid shallow breathing, weak, rapid, or irregular pulse, and ultimately, convulsions and death. Hyperthermia greatly increases metabolic oxygen demand and hyperthermia, in the face of hypoxemia, is a particularly serious complication. Rectal temperatures greater than 40°C are cause for concern, and attempts should be made to cool the animal. Rectal temperature in excess of 41°C is an emergency and should be treated aggressively. Treatment in the field may include moving the animal into shade, or spraying with cold water. Pack ice or snow around the animal, and consider cold water enemas.

Supplemental inspired oxygen should be considered to optimize arterial oxygen content as oxygen demand rises. Intravenous administration of cool fluids effectively decreases the body temperature but requires larger volumes than are usually available. Treatment is often not effective; generally the best option, in field situations, is to complete procedures rapidly, administer antagonists, and allow the animal to recover. Hyperthermia is best prevented by avoiding immobilization or capture on very warm days or limiting activities to the coolest part of the day. Avoid prolonged pursuit, keep stress to a minimum, and use the least severe method of physical restraint.



Figure 8.3 Cooling of a hyperthermic wolverine.

Protect the animal from high ambient temperatures and direct exposure to the sun.

Hypothermia is a concern when animals are immobilized during low ambient temperatures. It is most common in young animals, animals with small body masses and animals in poor body condition. Hypothermia is characterized by decrease in body temperature, to below 35°C. If unchecked it may result in prolonged recovery, acidosis, and arrhythmias. Causative factors of hypothermia include: Low ambient temperature, evaporative cooling from windchill, wetness, or precipitation and drugs that impair thermoregulation. Supportive procedures consist of an immediate attempt to increase body temperature by drying the wet animal, covering the animal and providing external heat sources such as hot water bottles. Hypothermia may be prevented by avoiding immobilization or capture on very cold days. Protect the immobilized animal from low ambient temperatures and exposure to wind and precipitation. Keep it warm and dry by covering with blankets or a sleeping bag. Minimize conductive heat loss by maintaining the animal insulated from direct ground contact.

Physical restraint can induce greater stress than chemical restraint (Cattet et al., 2003). Generally, physical capture and restraint can be very stressful for wild animals, and methods must be developed to reduce the stress response. Physical restraint should be of short duration and administration of sedatives or anesthetics are recommended to prevent or reduce distress (Arnemo, Moe, and Søli, 1993; Cattet et al., 2004; Oakley et al.,



Figure 8.4 Protection against low ambient temperature in a brown bear.



Figure 8.5 Darting from a helicopter may be less stressful than trapping in brown bears.

2004; Arnemo et al., 2005). Contrary to widespread belief, chemical immobilization from a helicopter is perhaps the least stressful capture method for a wide range of mammalian species (Cattet et al., 2003). In most circumstances, the animal can be rapidly approached and darted, and the stress response elicited is minimized.

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9

Thermoregulation

Jeff C. H. Ko and Gary West

INTRODUCTION

It is estimated that 60% to 80% of all post-operative patients experience hypothermia. Hypothermia occurs when heat production is less than heat loss. Hypothermia can be classified into primary or secondary based on the cause of the hypothermia (Oncken, Kirby, and Rudloff, 2001). Primary hypothermia results from a patient's exposure to a cold environment. Secondary hypothermia can result from the effects of anesthetic drugs or from illness, which alternates heat production and effects thermoregulation. Based on a retrospective study using 55 dogs and 77 cats, hypothermia was defined as mild (98 to 99.9°F), moderate (96 to 98°F), severe (96 to 92°F), or critical (less than 92°F). Hypothermia correlated with clinical signs of mental dullness, decreased heart and respiratory rates, decreased mean arterial blood pressure, central nervous system depression, and increased mortality rates. Many small animal patients suffer hypothermia during thoracic or abdominal surgical procedures. Heat loss also can be dramatic in large animals without the prevention or treatment of hypothermia (Tomasic, 1999). Avian species are homeothermic, with normal temperatures ranging from 37 to 42°C. Heat dissipation is accomplished with panting and gular flutter. Heat loss in birds during anesthesia can be rapid and dramatic. Hypothermia in avian patients can lead to decreased heart rates and cardiac instability. Reptile species are heterothermic and require external thermal support during anesthesia. Reptiles do not have the ability to regulate body temperature perianesthetically and require thermal support until they have fully recovered (Heard, 2001). Reptiles should be maintained near their preferred optimum temperature range. Also reptiles should be monitored closely post-operatively to prevent hyperthermia or burns. Thermal burns can occur more easily in reptiles that are dehydrated with poor peripheral perfusion (Heard, 2001). Hyperthermia can occur in anesthetized patients as well. Hyperthermia may occur with

prolonged, stressful inductions during high ambient temperatures. This is a common occurrence during wildlife capture. Pursuit of an animal for capture may lead to excessive stress, exertion, and trauma. These can all contribute to hyperthermia in immobilized wildlife. Also animals with thick hair coats are prone to being overheated with warming devices. Some mammals, including carnivores, lose heat through panting. Using circle or rebreathing systems can trap and reuse expired heat from the patient. Also, during hyperthermia there is increased production of carbon dioxide. Carbon dioxide will interact with soda lime and generate additional heat through a chemical reaction (Thurmon, Tranquili, and Benson, 1996). Malignant hyperthermia can also occur in pigs, dogs, cats, and horses. This syndrome is characterized by increased aerobic and anaerobic metabolism in patients. Patients produce abnormal amounts of heat, carbon dioxide, and lactate. This results in severe acid-base abnormalities. Certain anesthetic agents, including inhalants, may contribute to the development of malignant hyperthermia. Expired carbon dioxide concentrations and body temperatures must be monitored closely during anesthesia. Hypercapnia may be the first sign of impending malignant hyperthermia in susceptible species.

PERIOPERATIVE HEAT LOSS

Patient heat loss during the perioperative period can be classified into four types: evaporative, conductive, convective, and radiant. Animals being prepped for surgical procedures have their hair clipped or feathers plucked. These patients are then scrubbed with disinfectants and alcohol, which further enhances evaporative heat losses. Animals with wet hair are then exposed to the surgery table and further heat loss occurs through conduction on the cold surface. Intraoperatively, dry and cold inhalant anesthetic gases and oxygen in the patient's airway induce the loss of evaporative heat and moisture.

Appropriate oxygen flow rates are an important consideration to prevent excessive cooling in the operating room. Inhalant anesthetics also lower the patient's threshold response to hypothermia. Abdominal surgery induces radiant, convective, and evaporative heat losses. Intravenous fluids or lavaging fluids should be prewarmed before using them as they further reduce the body heat loss.

Postoperatively, transportation of the patient from the operating room to the recovery area is an additional source of heat loss. Often the warming devices used in the operating room are discontinued and the recovery area may not have warming equipment or may not have the equipment pre-warmed for the patient. Wet hair or feathers can become an additional cause of heat loss in the recovery area. Even large animals must have their body temperatures monitored and these patients should continue to receive thermal support during anesthesia and recovery (Tomasic, 1999).

Horses and other large animal patients that are recovered on cool, dry surfaces without supplemental heat lose body heat rapidly and may have prolonged anesthetic recoveries (Tomasic, 1999). Anesthesia induces hypothermia by inhibiting the patient's ability to thermoregulate. This inhibition reduces metabolic heat production, and inhibits the patient's ability to shiver. Some anesthetics such as acepromazine and inhalant anesthetics tend to induce peripheral vasodilation and worsen the radiant heat loss. Anesthesia and surgery represent a combination of heat loss and decreased heat production.

CONSEQUENCES OF HYPOTHERMIA

Hypothermia may affect the central nervous, cardiovascular, respiratory, gastrointestinal, and metabolic systems of the animal. Conscious or sedated animals vasoconstrict their peripheral vasculature, shiver, exhibit piloerection, or puff their feathers in the early stages of hypothermia during the perioperative period. Perioperative mortality and morbidity are increased when hypothermia occurs. When core body temperature falls below 94°F the animal's ability to thermoregulate is decreased and animals lose the ability to shiver. Peripheral vasoconstriction causes continual body heat losses and subsequently vasodilatation can result and core body heat continues to be lost. Prolonged recoveries are the most commonly seen central nervous system sign with perioperative hypothermia. Anesthetic drug metabolism and ensuing recoveries are significantly prolonged. When exogenous heat sources are provided to re-warm hypothermic patients, shivering may be resumed. Shivering may be one of the most severe consequences of hypothermia. Shivering increases myocardial oxygen consumption and can lead to complete cardiac standstill. It has been shown that shivering increases myocardial oxygen consumption 400% to

500%. Hypoxemia is a common consequence of hypothermia and shivering. Hypothermia shifts the oxygen dissociation curve to the left and decreases the down-loading of oxygen from hemoglobin to tissues. This may further prolong anesthetic recoveries and increase the chance for complications.

Hypothermia affects myocardial conduction and can cause myocardial irritability. Hypothermia also decreases cardiac output and blood pressure. During anesthesia, hypothermia-induced bradycardia may develop and it may not respond to anticholinergics. Ventricular arrhythmias, including ventricular fibrillation, could also occur during severe hypothermia. Hypoventilation, respiratory acidosis, and apnea may be sequelae of hypothermia during and after anesthesia. Hypothermia can also lead to clotting abnormalities and thrombosis. Gastrointestinal ileus may occur as a result of hypothermia. Decreased immune function may occur after prolonged hypothermia (Oncken, Kirby, and Rudloff, 2001).

MONITORING BODY TEMPERATURE

Body temperature is controlled by the hypothalamus; therefore, it is important to measure core body temperature. A temperature sensor placed on the tympanic membrane theoretically monitors the blood flow in the branches of the internal carotid artery. The internal carotid artery supplies the hypothalamus, and thus reflects core body temperature. A sensor placed in the lower one-third of the esophagus can measure the temperature of aortic blood. If the sensor is placed in the proximal or middle third of the esophagus, it is influenced by cool anesthetic gases in the endotracheal tube and can give a falsely lower reading. Rectal temperature readings measure local changes in temperature and they may depend on the regional blood flow and other factors. Rectal temperatures may be somewhat different from core temperature, but they may be a useful way of monitoring relative changes in body temperature.

PREVENTION AND TREATMENT OF PERIOPERATIVE HYPOTHERMIA

Frequently, rewarming of hypothermic patients becomes necessary, if preventative measure fail to prevent hypothermia. It has been suggested that a hypothermic patient should be actively re-warmed until a rectal temperature of 98.5°F is reached. Reptiles should be maintained near their preferred optimum temperature range during the perioperative period. During re-warming procedures, coagulation parameters, the cardiorespiratory system, electrolytes, acid-base status, and mental alertness should be monitored.

The use of heating devices or methods of providing heat can be classified as warming from body surface to the core (externally supplied) and from the core to the body surface (internally). Circulating heated water blankets and forced hot air warmers are typical warming devices that heat patients externally. Warm intravenous fluids, warm saline lavages, or warm water enemas are methods of warming a patient internally. All these methods have been shown to decrease heat loss.

In avian patients, radiant energy heat sources were found to be effective in preventing hypothermia in doves (Phalen, Mitchell, and Cavazos-Martinez, 1996); however, in a study with Amazon parrots, a forced air warmer was superior in maintaining body temperature when compared to infrared heater or circulating water blanket (Rembert et al., 2001). Heat loss still occurred in birds anesthetized for greater than 30 minutes, but temperatures were maintained in acceptable ranges (Rembert et al., 2001).

Commercially available fluid warmers can be used to warm fluids or blood immediately prior to infusion. Operating room temperature should be maintained at 71 to 73°F or slightly higher. Heating water circulating blanket and pumps should be turned used and their temperatures maintained at appropriate ranges (around 104°F) before the patient is anesthetized. The patient should be kept covered with towels or forced hot air quilt blankets during the perioperative period. Results from a study in dogs showed that using heated water blankets around the feet and legs was the preferable method of preventing heat loss (Cabell, Perkowski, and Greogor, 1997). This was compared with a heating blanket that is applied on the trunk of the anesthetized dogs. Forced hot air warmers can be effectively used to provide heat before, during, and after surgery. Forced hot air is filtered and delivered to the patient's skin through a convective quilt. The quilts have several configurations to accommodate incision site exposure and various patient positionings. The quilts can be placed under or on top of the patient. Most of the quilts are durable and can withstand extensive use, although they are designed to be disposable (Figure 9.1).

Anesthesia and surgery predispose patients to hypothermia. Management of perioperative hypothermia includes: properly monitoring the animal's body temperature, preventing heat loss, and providing heat supplementation. This reduces the morbidity and mortality of the patient during the perioperative period.

PREVENTION AND TREATMENT OF PERIOPERATIVE HYPERTHERMIA

If capture-related hyperthermia occurs in an immobilized animal, then immediate supportive measures should be used to lower the body temperature. Moving the animal to a cooler location, the use of cold water or ice topically, administering cool intravenous fluids, or cold water enemas may be tried. Supportive measures



Figure 9.1. Young dromedary camel postoperatively receiving supplemental heat from a forced air warmer. (Figure courtesy of Dr. Tomo Inohue, Department of Veterinary Clinical Sciences, Purdue University's College of Veterinary Medicine.)

may also include the treatment of shock and the administration of non-steroidal antiinflammatory agents. Animals should be cooled gradually down to 103°F, then cooling measures should stop. Rapid cooling can result in coagulation disturbances such as disseminated intravascular coagulation.

Immobilizing animals on warm days should be avoided when possible. Minimizing pursuit and capture times helps decrease stress-associated hyperthermia. Ventilation should be monitored closely and supported in hyperthermic animals.

A serious sequela of hyperthermia and capture is exertional rhabdomyolysis or capture myopathy. The reader should refer to Chapter 10 for more specific information about this potential complication.

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10 Capture Myopathy Jessica Paterson

INTRODUCTION

Capture myopathy (CM) is a non-infectious, metabolic disease of wild and domestic animals that can lead to significant morbidity and mortality. The condition is most commonly associated with pursuit, capture, restraint, and transportation of animals. Capture myopathy may also manifest secondary to other diseases, or as a result of natural hazards encountered in the environment. Capture myopathy is characterized by metabolic acidosis, muscle necrosis, and myoglobinuria. Clinical signs include muscle stiffness, severe muscle pain, ataxia, paresis, torticollis, prostration, and paralysis. Animals typically become obtunded, anorexic, and unresponsive. Death can occur within minutes or hours of capture, up to days or weeks after the inciting event.

Capture myopathy has been described in a remarkably wide range of vertebrate species, primarily within the mammalian and avian taxa. A very similar condition has been reported in poikilotherms, including fish (Holloway and Smith, 1982) and amphibians (Williams and Thorne, 1996). A recent study identified a condition resembling CM in lobsters (Stentiford and Neil, 2000). The disease has never been described in reptiles.

Capture myopathy shares many similarities with the myodegenerative disorders of domestic cattle, sheep, horses, and swine, as well as exertional rhabdomyolysis (ER) in humans. The factors that preclude the onset of capture myopathy can be highly unpredictable and the manifestations of the disease often vary among species and individuals. Treatment has a low success rate and a much greater emphasis has been placed on prevention.

HISTORY

Capture myopathy has been termed muscular dystrophy, white muscle disease, overstraining disease, capture disease, cramp, leg paralysis, spastic paresis, stress myopathy, transport myopathy, incipient myopathy, degenerative polymyopathy, muscle necrosis, and idiopathic muscle necrosis throughout the literature. The condition is now most commonly referred to as capture myopathy, exertional myopathy, or exertional rhabdomyolysis. One of the earliest reports of lesions consistent with capture myopathy was reported in a white-tailed deer (Odocoileus virginianus) in 1955 (Hadlow). The first description of the pathology of CM was in a Hunter's hartebeest (Damalisicus hunteri) (Jarrett, Jennings, and Murray, 1964). Throughout the late 1960s and early 1970s CM was described in many free-ranging African ungulates (Mugera and Wandera, 1967; Basson, McCully, and Kruger, 1971; Hofmeyr, Louw, and du Preez, 1973; Harthoorn and Van Der Walt, 1974). Capture myopathy in other African mammalian species, including baboons (McConnell et al., 1974) and flamingoes (Young, 1967) were also documented during the same time period.

The first documentation of CM in North America was most likely in mountain goats (*Oreamnos americanus*) in British Columbia (Hebert and Cowan, 1971). The condition in these mountain goats was described as white muscle disease, but more accurately fits CM. Capture myopathy was reported throughout the late 1970s in several species of North American ungulates, including white-tailed deer (Wobeser et al., 1976), elk (Lewis et al., 1977), moose (Haigh et al., 1977), pronghorn (Chalmers and Barrett, 1977), and bighorn sheep (De Martini De Martini and Davies, 1977).

THE HUMAN COMPARATIVE

Capture myopathy is very similar to exertional rhabdomyolysis syndrome described in people (Warren, Blumbergs, and Thompson, 2002). There are hundreds of causes of rhabdomyolysis identified in people that are classified as either being acquired or inherited (Warren, Blumbergs, and Thompson, 2002). Exertional rhabdomyolysis is one of eight forms of human acquired rhabdomyolysis (Warren, Blumbergs, and Thompson, 2002) and traditionally has been associated

with military training (Smith, 1968) and exhaustive endurance sports (Lin, Chie, and Lien, 2005). With the changing demographic of society, current research has recognized new exercise-related hyperthermic syndromes such as "white collar rhabdomyolysis" (Knochel, 1990), and raver's hematuria (Sultana and Byrne, 1996).

Rhabdomyolysis is one of the leading causes of acute renal failure (ARF) in human patients (Vanholder et al., 2000). Progression of rhabdomyolysis to myoglobinuria and ARF was first described in humans during the London Blitz (Bywaters and Beall, 1941). Civilians suffering from crush injuries died from ARF within 8 days of hospital presentation despite treatable, localized limb injury (Bywaters and Beall, 1941).

ETIOLOGY

Exertional rhabdomyolysis, or CM, in animals is distinguished from other types of rhabdomyolysis by its pathophysiology, as it affects both skeletal and cardiac muscles in response to extreme stress and muscular exertion (Williams and Thorne, 1996). Capture myopathy is a complex and multifactorial disease. Spraker (1993) theorized that CM is an inherent mechanism that facilitates a symbiotic relationship between predator and prey. The prey animal experiences a relatively quick and painless death after capture by its predator, thus allowing the predator to conserve energy.

Other authors argue that CM develops in wild animals after an unnatural degree of stress and physical exertion (such as experienced during hunting or live capture) for which they are maladapted (Harthoorn, 1980; Bateson and Bradshaw, 1997). These authors believe CM is an iatrogenic disease and does not develop under the conditions of stress and predation naturally encountered in the wild. Human research has shown that conditioning people to more intensive levels of exercise can reduce, but not eliminate, the risk of developing ER (Knochel, 1990). Chalmers and Barrett (1982) suggested that the stresses of fear and anxiety are the triggering mechanisms for CM that may be modified by genetic or acquired predispositions to the disease. These factors in turn may be exacerbated by iatrogenically induced circumstances such as overexertion, disturbance, excessive handling, transportation, and shock (Chalmers and Barrett, 1982).

PREDISPOSING FACTORS

There are many predisposing or contributing factors for capture myopathy. These factors can be placed into seven categories and remembered with the mnemonic SECONDS (Table 10.1).

Species

Prey species are considered the most susceptible to capture myopathy in the mammalian taxa, particularly

Table 10.1. Predisposing or contributing factors for capture myopathy.

S	Species
E	Environment
С	Capture-related
O	Other diseases
N	Nutrition
D	Drugs
S	Signalment

ungulates. Highly susceptible African species include zebra, giraffe, nyala, tsessebe, duiker, roan antelope, red hartebeest, eland, springbok, kudu, giraffe, and female impala (Ebedes, Van Rooyen, and Du Toit, 2002). North American species with increased susceptibility to CM include white-tailed deer (Beringer et al., 1996) and pronghorn (Chalmers and Barrett, 1977). Fallow and hog deer in Australia appear to be more excitable, and thus more susceptible to CM, than species such as rusa and samba deer (Presidente, 1978).

Among avian species, the long-legged wading birds are particularly predisposed to CM. The combination of struggle during capture, and restraint in bags or cages in which the birds cannot stand, makes these species very susceptible to CM (Green, 2003).

Environment

Environmental factors that can increase the incidence of CM include extremes in ambient temperature, rain, and high humidity. The need for animals to negotiate steep terrain, difficult footing, or water hazards can hasten the onset of CM also.

Capture-Related Factors Capture related factors that contribute to CM comprise the largest category. Capture techniques that involve high chase speeds, prolonged exertion without rest, excessive handling, prolonged restraint, restraint that promotes struggling from unnatural positioning, crating, transport, subjection to fear stimuli over periods of time, and renewed stresses, such as repeated moving and transport predispose animals to CM. Injuries induced by capture techniques, or by other animals, can also increase the incidence of CM.

Eccentric exercises (when muscles are lengthening while trying to contract), have been correlated to a higher incidence of ER in people (Lin, Chie, and Lien, 2005). This activity damages muscle fibers as a result of increased strain on muscle tissues (Lin, Chie, and Lien, 2005). Laboratory rats experience more severe rhabdomyolysis after running downhill, probably because of strenuous eccentric muscle contractions (Schwane and Armstrong, 1983).

Other Diseases

Underlying diseases and infections can make an animal more susceptible to capture myopathy. Severe worm and tick infections cause anemia and weaken the animal. Heartworms compromise cardiopulmonary circulation. Animals that have used water sources that have a high salt content may have preexisting renal damage (Ebedes, Van Rooyen, and Du Toit, 2002).

Signalment

Extremely old and extremely young animals may be the most susceptible to capture myopathy (Ebedes, Van Rooyen, and Du Toit, 2002). Human literature suggests that males have a higher risk of developing severe ER (Lin, Chie, and Lien, 2005). Some authors theorize that estrogens have a protective effect, therefore reducing the risk for women (Lin, Chie, and Lien, 2005). There is no CM literature that has studied the incidence of the disease between sexes. Among African ungulates, heavily pregnant animals are considered more susceptible to capture myopathy than non-pregnant females (Ebedes, Van Rooyen, and Du Toit, 2002).

Nutrition

Nutrition is one area commonly overlooked as a contributing factor to CM. Animals with a pre-existing vitamin E or selenium deficiency may be predisposed to developing rhabdomyolysis (Hebert and Cowan, 1971). Providing food, water, and nutritional supplements to captured animals, particularly during prolonged transport or upon reaching the new destination, may reduce the incidence of CM (Ebedes, Van Rooyen, and Du Toit, 2002).

Drugs

Rhabdomyolysis is a frequent complication of illicit drug consumption in humans and a frequent finding in drug-related deaths (Welte, Bohnert, and Pollack, 2004). It is estimated that toxins and drugs play a role in up to 80% of adult human cases of rhabdomyolysis (Gabow, Kaehny, and Kelleher, 1982). Opiates are one of the most frequently implicated in primary druginduced rhabdomyolysis (Warren, Blumbergs, and Thompson, 2002). Controversial human literature suggests that abuse of μ opioids may lead to rhabdomyolysis through a directly mycotoxic effect (Warren, Blumbergs, and Thompson, 2002).

Potent μ opioids such as fentanyl, etorphine, carfentanil, and thiafentanil are often used in combination with $\alpha\text{-}2$ agonists, butyrophenones, benzodiazepines, and cyclohexamines for wildlife capture. Wildlife species immobilized with opioid-based combinations frequently demonstrate side effects such as excitement (Haigh, 1990), spontaneous movement (Haigh, 1990), muscle rigidity (Haigh, 1990), hypoventilation, catecholamine release (Schumacher, Citino, and Dawson, 1997), and hyperthermia (Jessup, 1984). These effects, combined with hypoxemia and elevated fluid loss, may significantly increase the risk of CM. It is important to recognize that non-opioid drug combinations can also

cause similar side effects and predispose anesthetized animals to CM (Caulkett et al., 2000). Animals immobilized with neuromuscular blockers such as succinylcholine can experience acute, severe onset of muscle rigidity, hypoxemia, and hyperthermia. These animals are at very high risk for CM.

PATHOPHYSIOLOGY

Spraker (1993) described the pathogenesis of CM as involving three primary components: perception of fear, sympathetic nervous and adrenal systems, and muscular activity. The normal physiology related to these components was described in detail by Spraker (1993) and is not repeated here. The pathophysiology of CM also has been extensively discussed by Chalmers and Barrett (1982), Spraker (1993), and Williams and Thorne (1996) and therefore is not discussed in detail in this chapter. In general, CM results from altered blood flow to the tissues and exhaustion of normal aerobic energy, particularly in skeletal muscle. Exhaustion of ATP in muscle cells leads to decreased delivery of oxygen and nutrients, increased production of lactic acid, and inadequate removal of cellular waste products (Spraker, 1993). Damaged muscle cells undergo necrosis to a varying degree. Myoglobin released from these cells cause tubular necrosis in the kidneys and acute renal failure (Vanholder et al., 2000). Similar necrosis of cardiac tissue can occur as well (Williams and Thorne, 1996).

CLINICAL AND PATHOLOGICAL SYNDROMES

Rhabdomyolysis literally means "dissolution of striped (skeletal) muscle" (Warren, Blumbergs, and Thompson, 2002). Exertion-induced rhabdomyolysis leads to the breakdown of skeletal muscle fibers with leakage of intracellular contents, including creatinine kinase (CK) and myoglobin into the blood. Current diagnosis of rhabdomyolysis in humans requires the presence of tetraparesis, CK elevation more than 10 times the upper reference limit, myoglobinuria, hyperkalemia, and coagulopathy (Melli, Chaundry, and Cornblath, 2005). A CK concentration greater than 10,000 U/L in horses is indicative of myopathy (Volfinger et al., 1994).

Despite the common mechanism of muscle breakdown, CM can manifest differently and have varying sequelae depending on the species, the individual, and the circumstances. One classification system defined four temporal syndromes of CM: hyperacute, acute, subacute, and chronic (Harthoorn, 1973). Spraker (1993) also described four primary CM syndromes: acute death syndrome, ataxic myoglobinuric syndrome, ruptured muscle syndrome, and peracute death syndrome. The latter classification scheme is discussed in detail in this chapter. When classifying specific clinical signs and gross and histological findings into different syndromes of CM, it is important to recognize that the

pathogenesis of CM is a continuum, and some animals may show clinical signs and pathology that overlap one or more syndromes.

Capture Shock Syndrome

Capture shock can occur during immobilization or within a short time after capture. Death usually occurs within 1 to 6 hours post-capture. Clinical signs include depression, hyperpnea/tachypnea, tachycardia, elevated body temperature, weak thready pulses, and death. Serum biochemical findings include elevations in serum aspartate aminotransferase (AST), creatinine phosphokinase (CK), and lactate dehydrogenase (LDH) enzymes. The most common postmortem lesions include severe small intestinal and hepatic congestion along with pulmonary congestion and edema. Frank blood and blood-tinged contents may be found within the lumen of the small intestine.

Histological findings may include small areas of necrosis in skeletal muscle, brain, liver, heart, adrenal glands, lymph nodes, spleen, pancreas, and renal tubules. These lesions are most pronounced if the animal was hyperthermic. Small thrombi are found occasionally in the capillaries in various organs (Spraker, 1993).

Ataxic Myoglobinuric Syndrome

The literature suggests that this is the most commonly observed among the four syndromes. It may become evident several hours to several days post-capture. Clinical signs may include mild to severe ataxia, torticollis, and myoglobinuria. Serum enzymes (AST, CK, and LDH) and blood urea nitrogen (BUN) levels are elevated. Animals demonstrating mild signs are the most likely to survive. Animals with moderate to severe symptoms have a higher mortality.

Gross lesions can be seen in the kidneys and skeletal muscle. The kidneys are swollen and dark. The urinary bladder is empty or contains a small amount of brownish urine. The cervical and lumbar muscles, as well as the flexor and extensor muscles of the limbs (appendicular skeleton) contain multifocal, pale, soft, dry areas, accentuated by small white foci in a linear pattern. The lesions are bilateral but not symmetrical. They are subtle in animals that die within 1 to 2 days after capture, but they are more pronounced in chronic mortalities. Animals with prolonged survival may have small ruptures within the necrotic muscles.

Histological lesions are primarily localized to the renal cortex and skeletal muscle. Renal lesions are characterized by dilatation of tubules, moderate to severe tubular necrosis, and protein (myoglobin) casts. Muscular lesions are characterized by acute rhabdomyolysis. Myocytes are markedly swollen, with loss of striations and fragmentation and cleavage of myofibrils. Sarcolemmal nuclei are pyknotic in multiple areas. Sarcolemmal proliferation usually begins within 3 days of capture (Spraker, 1993).

Ruptured Muscle Syndrome

Clinical signs of this syndrome do not usually manifest until 24 to 48 hours post-capture, and animals initially appear normal. Physical examination findings include a marked drop in the hindquarters and hyper-flexion of the hock because of unilateral or bilateral rupture of the gastrocnemius muscle. Extreme elevations in AST, CK, and LDH are present. BUN may be within normal limits or slightly elevated. Although most animals with ruptured muscle syndrome die within a few days, some may survive for several weeks.

Gross examination reveals massive subcutaneous hemorrhage of the rear limbs, and multifocal small to large, pale, soft lesions in the forelimb, hind limb, diaphragm, cervical, and lumbar muscles. Muscular lesions are similar to those described for the ataxic myoglobinuric syndrome but are more severe and widespread. Lesions are bilateral but not symmetrical. Multiple, small to large ruptures may be found in necrotic muscle bodies. The gastrocnemius, subscapularis, middle and deep gluteal, semitendinosus, and semimembranosus muscles are often ruptured.

Histological lesions are primarily located within the skeletal muscles and are characterized by severe, diffuse necrosis. More extensive sarcolemmal proliferation, fibrosis, and muscular regeneration are evident in ruptured muscle syndrome compared with the ataxic myoglobinuric syndrome (Spraker, 1993) (Figure 10.1).

Delayed-Peracute Syndrome

This syndrome is rare but can be seen in animals that have been in captivity for at least 24 hours. The animals appear normal if they are left undisturbed. When disturbed, captured, or acutely stressed, they try to escape or run but stop abruptly and stand or lie still for a few moments. During this period, their eyes begin to dilate



Figure 10.1. Yearling moose that developed capture myopathy after being trapped in a well for several hours. On presentation, the moose was unable to bear weight on his hind limbs and was placed in a sling.

and death ensues within several minutes. These animals die in ventricular fibrillation and have elevated AST, CK, and LDH. There are usually no lesions, or a few small pale foci within the skeletal muscle at necropsy. Histological lesions are characterized by mild to moderate rhabdomyolysis throughout the skeletal muscle, especially in the hind limbs (Spraker, 1993).

A syndrome called delayed acute capture myopathy was identified in three roe deer (Montané et al., 2002). These deer died 48 hours, 72 hours, and 8 days post-capture while being housed in a large enclosure. The authors reported no clinical signs of CM in the deer after capture or while housed in the enclosure until an unobserved, human-initiated pursuit took place. The animals most likely died 14, 41, and 21 hours after the disturbance, respectively. Although the etiology is similar to delayed peracute syndrome, there may be a different pathogenesis.

DIFFERENTIAL DIAGNOSES

Differential diagnoses for capture myopathy in wildlife may include white-muscle disease, plant toxicities such as *Cassia occidentalis*, *C. obtusifolia*, and *Karwinskia humboldtiana* (Chalmers and Barrett, 1982), malignant hyperthermia, early tetanus, hypocalcemia, and myositis. This is not an exhaustive list. Proper diagnosis of CM depends on history, clinical signs, clinical pathology, and gross and microscopic pathology (Chalmers and Barrett, 1982).

TREATMENT

As mentioned, treatment is generally considered ineffective for CM. Costs and logistics associated with treating wild animals, particularly in field situations, must be considered also. Several treatment options have been used in wildlife, or may be an option, and they are discussed here.

Analgesia

Animals suffering from capture myopathy can experience severe muscle pain. Analgesia should be considered from an ethical and prognostic point of view. The distress and anxiety resulting from pain make this disease more difficult to treat. Analgesics used vary depending on the affected species. Judicious use of non-steroidal antiinflammatories is an option provided there is no indication of renal damage. Opioid administration with or without a sedative should be considered also. Corticosteroids may alleviate pain and help preserve lysosomal membrane and capillary integrity.

Dantrolene

Dantrolene sodium is a lipid soluble hydantoin analogue used to treat and prevent malignant hyperthermia in humans and exertional rhabdomyolysis in horses

(McKenzie et al., 2004). Dantrolene suppresses the release of calcium from the sarcoplasmic reticulum (Krause et al., 2004). Side effects associated with dantrolene include neurological deficits, muscular weakness, and hepatoxicity (McKenzie et al., 2004). There are no reports of dantrolene being used to treat CM and it would be impractical for field use because of its light sensitivity, insolubility, and expense (McKenzie et al., 2004).

Benzodiazepines

Benzodiazepines, including diazepam, midazolam, and zolazepam, are centrally acting muscle relaxants that produce excellent muscle relaxation, and reduce muscle spasms and spasticity (Muir, Hubbell, and Skarda, 2000). Benzodiazepines are anticonvulsants and may produce calming effects in obtunded and/or debilitated animals (Muir, Hubbell, and Skarda, 2000).

Multivitamins

Parentrovite was a balanced formulation of B vitamins with vitamin C in parenteral form. The drug was withdrawn from the human market in 1989. Parentrovite was administered to tsessebe to treat locomotory and capture stress but no conclusions could be made as to its effectiveness (Harthoorn, 1976).

Pabrinex is the only commercial multivitamin preparation currently available for parenteral use in the United Kingdom. The formulation contains thiamine, riboflavin, pyridoxine, nicotinamide, and vitamin C. Pabrinex has been associated with anaphylaxis when administered to human patients.

Hyperbaric Oxygen

Hyperbaric oxygen has been used as an adjunctive therapy in humans for severe rhabdomyolysis and acute renal failure (Abdullah, Al-Waili, and Butler, 2006). Hyperbaric oxygen (HBO₂) induces high oxygen partial pressure in all tissues, inhibits toxin formation, and promotes wound healing (Abdullah, Al-Waili, and Butler, 2006). The popularity of this therapy in veterinary medicine is increasing and may become more accessible in the future, particularly for highly valued zoo animals.

Sodium Bicarbonate

Sodium bicarbonate is used to treat acidemia and alkalinize the urine. Approximately 4 mEq/kg of sodium bicarbonate administered intravenously was successful in resolving metabolic acidosis and reducing mortality in captured zebra (Harthoorn and Young, 1974b). Alkalinizing the urine can reduce the risk of tubular obstruction by myoglobin casts; however, myoglobin is also intrinsically nephrotoxic (Lane and Phillips, 2003). Blood gas analysis should be used to titrate bicarbonate therapy ideally. The practicality of using this therapy in the field is limited.

Fluid Therapy

Intravascular volume expansion with balanced electrolyte solutions is effective in treating metabolic acidosis, hyperkalemia, dehydration, and myoglobinuria. Intravenous fluid therapy would also help to offset hypotension that occurs in some cases of CM.

PREVENTION

Possible modes of preventing CM depend largely on the species being captured, the goal of capture, the resources available, and the environment in which the capture is taking place. Operators must recognize environmental limitations such as extremes in temperature or terrain. Wildlife should be minimally handled by experienced workers. Transportation needs to be as brief as possible and appropriate for the species and individual. Wild animals also adapt better to capture and confinement with prior training and desensitization.

Drugs chosen for immobilization should be tailored for rapid induction, rapid recovery, efficient delivery, and physiological stability. Duration of anesthesia should be as short as possible and oxygen supplementation is always recommended. Administration of phenothiazines, such as acepromazine (Montané et al., 2003), or long-acting α -2 agonists, such as zuclopenthixol acetate (Read, Caulkett, and McCallister, 2000), can aid in reducing stress during transport, handling, and confinement.

The following study provides a case-specific, yet universally applicable, example of how CM can be minimized (Harthoorn, 1980). From 1973 to 1978 the mortality rate in captured and relocated animals in Traansval provincial reserves in South Africa dropped from 15% to 1.1% (Harthoorn, 1980). The high mortality rate was attributed to net capture with prolonged restraint, the capture of individuals rather than family groups, individual crating and transport, prolonged holding in slatted pens, further handling and transport after a rest period, and a sudden change in food. Survival rates were improved by reducing chase speeds, allowing periodic rests during drives over long distances, an almost a total absence of handling, capturing family or herd groups, transporting to the destination immediately after capture with no holding or quarantine, using plastic sheeting or Hessian funnels and corrals, reducing fear and stress by eliminating shouting and other noise, and ensuring minimal contact between the animals and capture personnel.

CONCLUSIONS

Capture myopathy remains a frustrating and poorly understood condition despite its generous representation in veterinary literature. Its unpredictable and multifactorial nature poses a distinct challenge to those who study the disease. Developing an effective treatment for

CM will require a better understanding of how to stop the physiological cascade once it has been triggered. The key to preventing CM lies in understanding the behavior and physiology of individual species. Wildlife intervention must be carried out with great planning and precision and, ultimately, the welfare of the animal must always be the first priority.

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11

Human Safety during Wildlife Capture

Nigel Caulkett and Todd Shury

INTRODUCTION

Capture and anesthesia of zoo and wild animals is inherently dangerous for personnel. These risks can be elevated in free-ranging situations in which the capture team may be subject to environmental threats. Prior to any capture, procedure steps must be taken to recognize potential risks to personal safety, and every attempt should be made to reduce the risk of injury. In the event of injury there must be a well-thought-out treatment and evacuation plan to deal with the situation.

This chapter discusses some of the major risks to human safety that may be encountered during the capture and handling of wildlife. It discusses methods to reduce risk, and explains how to prepare for and deal with emergency situations.

RISKS TO HUMAN SAFETY DURING WILDLIFE CAPTURE AND HANDLING

Environmental Risks

Before working in any environment, it is important to be aware of potential hazards. Weather conditions can pose a risk, particularly in areas where personnel may be exposed to extremes of temperature. In some environments the weather may change very quickly; heavy fog or snow can disable helicopter flight and leave a crew stranded. Personnel should be well prepared for the weather conditions and terrain that may be encountered in their environment. In areas that have rapidly changing weather conditions clothing should be carried to protect them from adverse weather conditions. Adequate water supplies are vital in any environmental condition. In remote areas personnel should be prepared to spend the night outdoors if it is not possible to return to base. Altitude can be a problem if personnel are not properly acclimated. Personnel should be aware of potentially dangerous mammals, reptiles, or insects in a given environment. The availability of potable water can be a concern. Communication is vital in emergency situations and a reliable method of communication should be established. In areas in which cellular phones do not function, VHF radios may be an option. Satellite telephones function in most parts of the world.

Disease risks should be evaluated for a given environment, and steps should be taken to prevent exposure to infectious disease. Public health professionals should be consulted to determine disease threats and vaccine requirements or malaria prophylaxis in a given region. In some environments the political situation can be hazardous. Capture personnel should be aware of human-related risk factors in a given environment.

Equipment-Related Risks

Remote Delivery Equipment Dart rifles and pistols have the potential to induce severe trauma if they are used inappropriately (Bush, 1992; Cattet, Bourque, and Elkin, 2005). They should be treated with the same respect as firearms. Personnel using dart rifles and pistols should have appropriate firearms training and practice firearms safety rules.

Dart loading is a potentially hazardous procedure. The risk of drug exposure is increased during dart loading and during charging of darts that use compressed gas for their discharge. Darts should never be loaded alone, and should always be loaded on a steady surface (i.e., never in a moving vehicle). There should be sufficient water available to dilute spills, and protective clothing (i.e., safety glasses, gloves, overalls) should be worn to prevent exposure to drugs. Darts should always be covered, to contain leaks, when they are charged. Loaded darts should always be stored in a sealed, impenetrable, leakproof container (Figure 11.1).

Firearms A firearm backup is essential when working with potentially dangerous animals. Everyone working around firearms should receive firearms safety training, and only very experienced personnel should be in charge of providing the firearm backup. It is important



Figure 11.1. Safe dart loading.



Figure 11.2. Firearms backup.

to choose a firearm that has sufficient impact energy to rapidly incapacitate the target species.

In some situations animals other than the immobilized animal may be the major threat. In these situations it is advisable to assign a dedicated person to the task of guarding the capture crew (Figure 11.2).

Compressed Gas Care must always be taken when transporting or delivering oxygen. Aluminum D or E cylinders can be easily transported in the field. It is important to secure the tanks, as impact damage to the neck of the cylinder can result in a rapid escape of gas and create a missile. Oxygen should never be used around open flames or grease. People using compressed gasses should have appropriate safety training.

Traps and Snares Traps, snares, and nets are frequently used to facilitate physical capture. Net guns have the potential to induce severe injury if the victim is struck



Figure 11.3. Helicopter safety training.

by a weight. Net guns are frequently used from a helicopter. Nets have the potential to induce a crash if they are deployed into the main or tail rotor (National Transportation Safety Board, 2002).

Leg hold traps and snare springs can produce significant bruising or crush injuries. Culvert traps that have heavy guillotine-type doors can induce significant injury.

Helicopters Wildlife capture work often involves low-level highly technical flying. Capture may occur at altitude and sometimes in inclement weather. Helicopter crashes have been a significant cause of injury and death during wildlife capture work (Jessup et al., 1988). A highly skilled, experienced pilot and a well-maintained aircraft is vital in these situations. It is also very important to make safe decisions about the weather conditions before embarking on a capture expedition.

Personnel working around helicopters should receive safety training (Figure 11.3). Helmets and fire-proof clothing may decrease the risk of mortality during a helicopter crash.

Animal-Related Risks

Trauma Animal-induced trauma is very frequent in personnel working with zoo and wild animals. In 1998 a special report in the *Journal of Zoo and Wildlife Medicine* reported a 61.5% incidence of major animal-related injuries in zoo veterinarians (Hill et al., 1998). The most frequently reported injuries were animal bites and kicks. Scratches, crush injuries, and horn wounds also were reported. This report recommended the use of long-sleeved shirts, lab coats, leather gloves and face shields to protect from injury (Hill et al., 1998).

Zoonotic Infections Zoonotic infections are relatively common in zoo and wildlife workers. These infections range from simple irritations to life-threatening conditions. The above study quoted a 30.2% incidence of

zoonotic disease in zoo veterinarians. The most common infection was ringworm (reported by 28 veterinarians), followed by psittacosis (24 veterinarians) (Hill et al., 1998). Careful handling, protective clothing, and up-to-date vaccination status are important to prevent the transmission of zoonotic disease. Effective human vaccines are available for rabies prophylaxis when exposure to carnivores or bats is likely (Centers for Disease Control and Prevention, 1999).

Drug-Related Risks

Anesthetic Gases Anesthetic gases are commonly used by zoo veterinarians. Ninety-one percent (91%) of zoo veterinarians have reported using inhalant anesthetics, and 10.9% reported an adverse exposure (Hill et al., 1998). The most commonly reported effects with halothane and isoflurane were headaches, dizziness, sleepiness, and light-headedness (Hill et al., 1998). Nitrous oxide exposure was associated with dizziness and sleepiness. Chronic occupational exposure to nitrous oxide has been associated with decreased fertility and increased rate of abortion in dental assistants (Rowland et al., 1992).

Occupational exposure to all gas anesthetics should be minimized. The best method to minimize exposure is the use of an active scavenging system. In addition to active scavenging, delivery equipment should be well maintained to minimize leaks. It is further recommended that anesthetic gas exposure should be periodically monitored by an industrial hygienist (Hill et al., 1998).

Drugs Used for Remote Delivery Drugs designed for remote delivery are often very potent. Although this allows for the delivery of small volumes it also increases the risk of intoxication from exposure to the drug. Capture drugs must always be handled with respect and the level of vigilance always must be high. It is a good practice to always wear gloves when drugs are handled. A face shield is also recommended when working with potent narcotics. Coveralls can be quickly removed if a drug is spilled on them. If a human antagonist is available it should be drawn up and ready to administer. One should never work alone, and everyone on the capture team should be trained in first aid and CPR. It is important to maintain an increased level of vigilance during the handling of drug vials, the loading and unloading of darts and during pressurization of darts that use compressed air for injection.

Potent Narcotics Potent narcotics are commonly used for the capture and handling of ungulates. They are a group of drugs that demand respect and care in handling. The three drugs in common usage are etorphine, carfentanil, and thiafentanil. Carfentanil has been quoted to be 10,000 times as potent as morphine (Van Bever et al., 1976). Thiafentanil has been quoted to be

6,000 times the potency of morphine (Stanley et al., 1988). Not only are these drugs potent, but they are also formulated in a relatively concentrated solution to increase their utility for remote delivery. Carfentanil is commercially available as a 3 mg/ml solution. Thiafentanil is typically used as a 10 mg/ml solution. These factors, taken together, increase the risk of a significant human intoxication with exposure to a very small volume of drug.

There are several reports of human intoxication in the literature. Most of these reports detail human intoxication with etorphine (Anon, 1976; Summerhays, 1976; Sheridan, 1981). One human fatality was reported from accidental injection of etorphine (Anon, 1976). There is very little information concerning human intoxication from carfentanil or thiafentanil. It is likely that minor intoxications are not reported because of embarrassment (Haigh, 1989).

The ultrapotent narcotics have a high therapeutic index in comparison with older drugs, such as morphine (Wax, Becker, and Curry, 2003). The therapeutic index of carfentanil in rats is 10,600 (Van Bever et al., 1976). It has been argued that the high therapeutic index may confer a higher level of safety in the event of human exposure. In October of 2002 the Russian military used an "incapacitating gas" to end a hostage crisis at the Moscow Dubrovka Theater. The gas was most likely a mixture of carfentanil and halothane (Wax, Becker, and Curry, 2003). Unfortunately, 127 of the 800 hostages died and 650 of the survivors required hospitalization. Given the high therapeutic index, this number of deaths was not anticipated by Russian officials (Wax, Becker, and Curry, 2003). Obviously it was not appropriate to directly extrapolate animal data to human beings (Wax, Becker, and Curry, 2003). This incident stresses the need for a high level of vigilance when these agents are used.

Given the potential risks of these agents and their widespread use, it is surprising that there are very few published reports of accidental human intoxication. It is possible that this is the result of education and safe practice by zoo and wildlife veterinarians. A survey found that 65.1% of zoo veterinarians reported using ultrapotent narcotics and immobilizing agents (Hill et al., 1998). Of those who used these drugs, 86.7% had a written emergency protocol, 92.3% wore gloves, and 76.2% wore eye protection (Hill et al., 1998). This good standard of practice probably limits the incidence of adverse drug exposure in zoo veterinarians.

Prevention of exposure to potent narcotics is the best way to avoid intoxication. Protective clothing, gloves, and an eye shield should always be worn when these drugs are handled. Full face protection can be advantageous to prevent oral, ocular, or nasal exposure.

Symptoms of narcotic overdose in humans include nausea, dizziness, respiratory depression, and miosis. This can progress to coma and cardiovascular collapse

with severe intoxication (Haigh and Haigh, 1980). Rapid administration of a specific narcotic antagonist is vital in the face of severe intoxication. Naloxone has been advocated for this purpose, but it must be administered at a high dose, and because of its short half-life, repeated dosing is probably required. A dose of 0.53 to 2 mg/kg of naloxone may be required to antagonize the effects of carfentanil in humans (Petrini et al., 1993). This may require up to 14 10-ml vials of 1 mg/ml naloxone (Petrini et al., 1993). Naltrexone is commonly used to antagonize potent opioids in wildlife (Allen, 1989). It has the advantage of a long half-life, which reduces the risk of renarcotization following antagonism of carfentanil (Allen, 1989). Naltrexone is available as a 50-mg tablet for human use. It is advocated for the treatment of narcotic addiction and alcoholism. An oral formulation is less useful than an injectable form in emergent situations, particularly when intoxication may include nausea, vomiting, or coma. The oral formulation of naltrexone could prove useful after initial antagonism with naloxone, particularly in remote locations in which medical help is difficult to access.

Intoxication from a large dose of an opioid can occur very rapidly. Personnel should always work in teams and everyone should be trained in first aid with a current CPR certificate. The major threat to life from opioid overdose is from respiratory depression. A means of assisting respiration such as rescue breathing with a pocket mask or Ambu bag can provide the respiratory support that is required until the intoxication is treated. If oxygen is available, it should also be used during rescue breathing.

α-2 Agonists There are several published reports that detail human deaths or intoxication from xylazine (Carruthers, Wexler, and Stiller, 1979; Fyffe, 1994; Capraro, Wiley, and Tucker, 2001). In most of these reports xylazine was self-administered, either in a suicide attempt or for recreational use. Intoxication is commonly characterized by bradycardia, hypotension and respiratory depression. Treatment of xylazine intoxication is typically supportive care and the use of assisted or controlled ventilation (Carruthers, Wexler, and Stiller, 1979; Fyffe, 1994; Capraro, Wiley, and Tucker, 2001). α-2 Antagonists such as yohimbine and tolazoline are not typically used to treat xylazine intoxication in humans.

The use of xylazine has been widespread in veterinary medicine. It has proved to be an extremely useful drug for wildlife capture and handling. In recent years there has been a drive to develop α -2 agonists with increased potency and specificity for the α -2 receptor. Medetomidine has proved to be a very effective drug for wildlife capture and handling. It can be formulated in a concentrated solution of 10 to 20 mg/kg. This concentration, combined with its high potency, makes medetomidine very attractive for wildlife handling. This same factor increases the risk of human intoxication with a very small volume exposure. Dexmedetomidine is the

pharmacologically active *d*-isomer of medetomidine. Dexmedetomidine is marketed in the United States as Precedex (Hospira, Inc., Lake Forest, IL). Precedex is typically administered as an intravenous (IV) loading dose of 1 µg/kg, followed by an infusion of 0.2 to 0.7 µg/kg/hour. Side effects at this dose include transient hypertension (during the loading dose), bradyarrhythmias, and hypotension. This dose is used to induce sedation and facilitate ventilation of ICU patients. An IV dose of 75 µg (total) induced significant bradycardia and an 18% reduction in blood pressure (compared with baseline) in human volunteers (Kallio et al., 1989). This dose is equivalent to approximately 150 µg of medetomidine. If medetomidine is formulated to a concentration of 10 mg/ml, this dose will be contained in 0.015 ml of solution. It is obvious from this example that the formulation of medetomidine routinely used in wildlife anesthesia is extremely potent and deserves the same degree of respect given to potent opioids.

Treatment of exposure to a toxic dose of an α -2 agonist is supportive. In a field situation the victim may benefit from administration of supplemental inspired oxygen and ventilatory support as needed. Airway protection is important as well if the victim becomes comatose. Heart rate and blood pressure should be monitored. Rapid evacuation to a medical facility is vital for the victim to receive appropriate treatment for hypotension and respiratory depression.

Phencyclidine Derivatives Two phencyclidine derivatives are commonly used for wildlife anesthesia. Ketamine is typically used in combination with an α -2 agonist or benzodiazepine tranquilizer. Telazol is a 1:1 combination of tiletamine, an arylcyclohexamine structurally related to phencyclidine and zolazepam, a benzodiazepine tranquilizer. There are case reports that detail human fatalities with self-administration of telazol (Cording et al., 1999; Chung et al., 2000). These drugs are typically used to produce a state of dissociative anesthesia. One of the major side effects of ketamine is bizarre hallucinations, which have limited its utility in human anesthesia. Ketamine is a common drug of abuse. Its effects appear rapidly and include visual hallucinations and a dreamlike state (Gahlinger, 2004). Undesired side effects include: confusion, delirium, tachycardia, palpitations, hypertension, and respiratory depression (Gahlinger, 2004). Severe intoxication results in loss of consciousness and the accompanying risks of respiratory depression or airway loss.

Ketamine is often snorted, with a typical abuse dose of 20 mg into each nostril (Stotter Cuddy, 2004). It can be seen from the preceding discussion that a relatively low-dose exposure of ketamine or tiletamine could produce intoxication. A low-dose intoxication that resulted in confusion or disorientation could prove hazardous in a wildlife capture environment. In the event of low-dose intoxication, the victim should be removed from the

capture team, reassured, closely monitored, and evacuated to a medical facility for observation. In the event of high-dose intoxication, the unconscious victim should receive supplemental oxygen, airway support, and rescue breathing if required. The victim should be rapidly evacuated to a medical facility for treatment.

EMERGENCY PREPAREDNESS

Every effort should be made to identify the risks associated with a planned capture procedure. It is always best to take steps to minimize the risk of human or animal injury. A pre-immobilization plan identifies risks, and allows the capture team to anticipate complications and take steps to mitigate those risks. Unfortunately, risk reduction is not always 100% successful; therefore, it is vital to develop an emergency response protocol that can be initiated if an accident occurs.

Pre-Immobilization Plan

A pre-immobilization plan should identify potential risks associated with a capture event or research project. Many of these risks are outlined in the preceding. All members of the capture team should be briefed on these risks prior to the capture. The plan should outline everyone's role on the capture team. A team leader is typically identified. The plan should ensure that everyone on the capture team is appropriately trained in wildlife handling techniques. Anyone working directly with the animal should receive appropriate training in chemical immobilization. Ideally, everyone on the team should receive training in first aid and hold a current CPR certificate. If this is not possible, at least two team members should have this training. Personnel should be trained in the proper use of darting equipment. Helicopter safety and firearms training may be indicated. Additional training may be required. This may include training in communications, survival, or terrain-specific training such as cold water survival or avalanche rescue. Field equipment should be checked prior to a capture event. First aid kits and human antidotes should be carried and team members must know how to access and use them. Appropriate clothing should be carried for the terrain and weather conditions.

A system of communications should be established between capture team members and any personnel required for evacuation or medical treatment of an accident victim. An emergency response plan needs to be developed. This plan must clearly outline the steps that will be taken in the event of an emergency. The plan should be well thought out and flexible enough to deal with any foreseeable emergency.

Emergency Response Protocol

An emergency response protocol should be developed prior to commencing work on a project and should be in place at any facility where there is a significant risk to human safety from wildlife or zoo animal capture and handling. These protocols are often quite specific for a facility or location, and need to be revised if wildlife capture is initiated in a new location. Good examples of specific emergency response protocols can be found in the literature (Petrini et al., 1993; Tolo and Keyler, 1998). The emergency response protocol should be developed in consultation with physicians who may be required to treat the victim and with emergency medical services (EMS) personnel who may be required to treat and transport the victim. The main components to the protocol are consultation with medical professionals, communication, treatment, and evacuation.

Consultation with Medical Professionals

In any true emergency, time to treatment is probably the most important factor that determines outcome. Emergency room physicians may not be familiar with drugs that are commonly used for wildlife capture. Development of an emergency response protocol should include a visit to the hospital that a victim will be evacuated to in the event of an emergency. Drug package inserts and information regarding the capture drugs should be given to the medical staff that may be required to treat the victim. The effects of most of these drugs can be extrapolated from similar drugs used in human medicine. The visit should also include a means to set up a communication link, from the field, to assist with initial stabilization of the victim. In some locations the victim may require evacuation by the capture crew. It is preferable to have the victim evacuated by EMS whenever it is available. The development of the emergency response protocol should include a visit to the ambulance service that would transport the victim. Ideally a paramedic should be dispatched to stabilize the victim. Stabilization in the field may include venous access and possibly intubation and ventilation. This treatment can be lifesaving. Again, the effects of the drugs and antagonists should be discussed.

Communication A reliable method of communication should be established with EMS and the hospital. This may be as simple as a cellular telephone. In remote locations VHF radios may be used, either directly to EMS or via a dispatcher. Satellite telephones are very useful for this purpose as they can be used from very remote locations. A communications link is vital in an emergency situation.

Treatment and Evacuation In the event of an emergency, timely treatment in the field will have a major influence on outcome. In remote locations, where access to EMS is difficult, capture team members should receive advanced first aid training. A first aid kit must be carried with appropriate equipment to treat a major traumatic incident. The accident victim should never be left alone, and help should be summoned as soon as possible. In

the event of drug intoxication, the key to a successful outcome will be the rapid administration of antagonists and supportive care. The unconscious victim should receive airway support and oxygenation. Rescue breathing can be lifesaving in the face of respiratory arrest. Rescue breathing can be learned through a CPR course. Ideally, advanced training should be taken to become certified in the use of pocket masks, oral airways, oxygen therapy, and Ambu bags, which facilitate ventilation with a high inspired concentration of oxygen.

An evacuation plan must be developed for every situation. Ideally EMS should be used for the evacuation. Paramedics and EMTs are experts in this field and can ensure that the victim is cared for appropriately during transport. In remote locations the capture team may need to evacuate the victim. The evacuation should be to the closest location for ambulance access, or directly to the hospital. If helicopters are used, it will be important to determine the best location for landing if there is not an established landing pad. The victim must never be left alone and should always be closely attended by someone who is trained in advanced first aid.

Capture and handling of wild animals is not without risk. It is vital to carefully plan for emergencies, as time spent planning and preparing for an emergency generally dictates the outcome.

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12 Capture and Physical Restraint of Zoo and Wild Animals

Todd Shury

INTRODUCTION

An important and often overlooked aspect of chemical immobilization of zoo and wild animals is proper physical restraint. How does one get close enough to be able to effectively and safely deliver the appropriate drug combination? Is it better to capture a group of animals or isolate individuals prior to immobilization? Would physical or chemical immobilization be more appropriate? The successful capture and restraint of wild species often requires a combination of physical and chemical restraint using a wide variety of capture and handling devices that are constantly evolving, and often there are no easy answers to these questions.

No single ideal capture or restraint technique can be successfully used for all occasions on a particular species because success depends on many biological, ecological, and practical factors, including topography, season, climate, age, condition, sex, costs, and logistics (Table 12.1). Many techniques for capture of free-ranging wildlife were developed in the latter part of the twentieth century and were extrapolated from zoos, wildlife parks, and the game ranching industry. This chapter primarily focuses on capture and restraint techniques for freeranging North American mammalian species, with more limited coverage of reptile, amphibian, and avian species in other parts of the world and captive situations. Properly applied physical restraint can be the most safe and efficient way to handle even large, dangerous animals if the people involved are knowledgeable about the likely behavior of the target animal(s) under stressful situations and are experienced with the technique being used.

There is tremendous overlap between the art and science of physically restraining wild animals so that they do not injure themselves or the people restraining them. Even when people are familiar with the techniques being used, certain people often just have the knack for restraining animals without undue injury and suffering. Much has been written and discussed on the

topic in the past thirty years with many old techniques being refined and simplified and completely novel techniques being used for the first time as new technologies become available (Fowler, 1995; Fowler and Miller, 2003). Many of the physical restraint techniques discussed are applicable to both captive and free-ranging wildlife, whereas the capture techniques primarily apply to free-ranging situations only. The information presented in this chapter is useful for biologists, veterinarians, technicians, and others who require techniques to safely and efficiently handle zoo and wild animals for a variety of management, research, treatment, and diagnostic reasons.

MAMMALS

Cervidae, Bovidae, and Antilocapridae (Artiodactylids)

Remote Capture Techniques Native cultures originally developed capture techniques for harvesting this group of animals and some of these techniques have been modified for live capture for wildlife research and intensive game farming over the past 30 years. Some techniques have been developed for mass capture, whereas others such as helicopter net gunning are designed for individual capture. Research on the comparative efficacy and level of morbidity and mortality associated with different capture techniques for wild artiodactylids is limited (Barrett, Nolan, Roy, 1982; Conner, Soutiere, and Lancia, 1987; Kock et al., 1987a,b; DeYoung, 1988; Scotton and Pletscher, 1998; DelGiudice, Mangipane, and Sampson, 2001), even though many thousands of animals have been captured using different methods.

Wild artiodactylids are trapped primarily for research, translocation projects, and population monitoring. Many techniques for physical restraint of domestic, zoo, and game-farmed cervids and bovids have been developed in North America recently (Haigh and Hudson, 1993).

Table 12.1. Comparison of physical capture techniques for free-ranging wildlife.

Technique	Cost ^a	Capture Efficiency ^b	Portability ^c	Potential for Injury ^d	Selectivity ^e	Species
Corral (boma) traps	Low	High	Low to moderate	Variable	Low	Ungulates, bovids, goats and sheep
Drive nets	Moderate to High	High	Low	Moderate	Low	Ungulates, bovids, goats and sheep
Helicopter net gun	High	High	High	Moderate	High	Ungulates, bovids, goats and sheep, ursids, canids
Drop/rocket net	Low	Moderate	Moderate	Moderate	Moderate	Ungulates, goats and sheep, birds
Foot hold traps	Low	Low	High	Low to moderate	Low	Canids, felids, mustelids
Foot snare	Low	Low	High	Low	Low	Birds, canids, felids, ursids, mustelids
Box traps	Low	Low	Low	Low	Low	Birds, most mammals
Cage traps	Low	Low	Low	Low	Low	Birds, most mammals
Mist nets	Low	High	High	Low	Low	Birds, bats

^aCost per animal captured on a relative basis.

Box traps are one of the most widely used individual capture techniques, consisting of a wooden or metal structure that is designed to trap a single animal so that it can be physically or chemically restrained. Designs have been developed for the capture of North American ungulates such as deer (Odocoileus spp.), elk (Cervus elaphus), moose (Alces alces), bighorn sheep (Ovis canadensis), and mountain goats (Oreamnos americanus) involving baiting animals into the trap followed by a mechanical or remotely operated device to close the trap. Animals are generally baited with hay, grain, fruit, or salt depending on local food preferences. Wooden box traps have been used for several decades in North America to trap white-tailed (Odocoileus virginanus) and mule deer (Odocoileus hemionus), bighorn sheep, and Rocky Mountain goats. These are essentially a plywood box with a top-hinged door or vertical guillotine slide that is tripped by either a floor plate or cross wire. These traps work best if there are few or no openings to allow light in, as darkness has a calming effect on trapped animals, causing them to struggle less. Once captured, animals can be either chased into a net placed over the opening to the trap and physically restrained or larger animals can be injected via pole syringe or blowpipe through a small opening. Care needs to taken to ensure that box traps are placed in relatively flat areas so the trapped animal does not roll down a slope and in areas that are not exposed to the elements.

Clover traps work on the same principle as box traps but are constructed of mesh netting over a steel tubular frame rather than a structure with solid walls. They have been used to successfully capture many ungulates in North America and are considerably lighter and more portable than most box traps because they can be easily collapsed for transport. Animals can be either physically restrained by collapsing the trap or chemically immobilized, depending on the extent of restraint required. An advantage of clover traps over box traps is the ability to place hobbles on an animal for physical restraint prior to removing it from the trap and traps can be checked from a distance without disturbing the animal inside. A disadvantage is that animals may be more exposed to adverse climatic conditions while trapped (e.g., snow, wind, and rain). Injuries and mortality can be sustained through capture of more than one animal in a trap or by appendages or legs being caught in netting material that is inappropriately sized. Clover traps are primarily used for capture of white-tailed deer, mule deer, and elk in North America using various baits such as hay, grain, or salt.

Helicopter net gunning was originally developed in New Zealand in the 1970s for capturing red deer (*Cervus elaphus*). It has become a favored method of capture for North American ungulates over the past 20 years because it can be adapted to a wide variety of animals, allows for selection of different age and sex classes, and large numbers of animals can be handled and captured in a short period of time relative to chemical immobilization (Jessup et al., 1988). It has been used for virtually every North American artiodactylid with varying degrees of

^bNumber of animals that can be quickly captured in a short period of time.

^cEase of changing to different capture locations quickly and efficiently.

 $^{^{\}rm d}\!\operatorname{Potential}$ for injury to the captured animal.

^eAbility to avoid capture of non-target species or individuals.

success. It is useful for short non-painful procedures such as application of radio telemetry collars and blood sampling without the need for chemical immobilization.

When painful procedures such as tooth removal or surgery are used with net-gunned animals, adjunct procedures such as local analgesia, sedation, or chemical immobilization must be used to provide adequate analgesia. Intranasal sedation with xylazine and reversal with yohimbine has been used successfully in elk (Cattet et al., 2004) captured by helicopter net gun.

Hobbles generally are applied to the ipsilateral front and hind limbs at the level of the metacarpophalangeal joints as a safety measure. Blindfolds are strongly recommended to reduce stress and calm the animal while being handled. Helicopter net gunning is not a viable option in heavily treed environments or excessively steep terrain because of lack of openings and risk of injury to the animal. Chase and hazing times need to be kept as short as possible to minimize risk of capture myopathy and hyperthermia. Hazing times are generally less than 10 minutes and chase times are generally less than 2 to 3 minutes. Temperatures in excess of 42.2°C are potentially life threatening for bighorn sheep (Jessup, 1999). Mortality from helicopter net gunning most commonly occurs as a result of cervical fractures and dislocations (Barrett, Nolan, and Roy, 1982), but can also result from capture myopathy and/or hyperthermia (Barrett, Nolan, and Roy, 1982; Kock et al., 1987a). This risk can be minimized by attempting to slow animals prior to net placement by turning them or waiting for deep snow conditions in northern areas.

Bovids and ungulates are generally only safely handled for short periods of 15 minutes or less in lateral recumbency with few complications. If longer periods of restraint are required, reversible sedation with an α -2 agonist delivered intranasally or intravenously should be considered as an adjunct procedure.

Net size should be appropriate for the species being captured with most nets being in the range of 9 to 17.6 m². A lightweight extremely strong material is required for net construction and durability (Barrett, Nolan, and Roy, 1982). Appropriate mesh size is also important to prevent the animal escaping prematurely and allow quick entanglement.

Net guns also can be fired from the ground for capture of antelope and other species (Firchow, Vaughan, and Mytton, 1986; O'Gara and Yoakum, 2004), but care must be taken to ensure that the weights do not hit the animal, causing severe injury. Net guns have been used from a helicopter to capture bighorn sheep, mountain goats, deer, elk, moose, bison, and antelope in North America. Advantages of net gun capture include rapid capture and ability to select animals, rapid immobilization so injuries can be avoided, and the ability to release animals quickly without drug residues. Disadvantages include lack of utility in heavily treed environments and potential for high mortality and morbidity.

Corral traps or bomas have been used extensively for the mass capture of most artiodactylid species in Europe, North America and Africa. This is perhaps the oldest and most widely used capture technique for ungulate species for purposes of translocation, research, and testing. The use of boma traps is well described in Ebedes, Van Rooyen, and du Toit (2002).

Drive nets are useful to capture ungulate and bovid species in which other techniques are not practical, such as heavily treed or steep terrain or in urban environments. Nets are typically strung between poles or trees in an area where animals can be flushed into a narrow opening or other suitable area. It is critical that adequate numbers of people are available to physically restrain animals once they are entangled in the net. One or two people per animal are generally required depending on the size of animals captured.

Animals can be driven into nets on foot, by horse-back, or by vehicles (snowmobile or truck) or aircraft (helicopter or fixed wing). Care must be taken when using aircraft or vehicles that animals are not chased at excessive speeds or long periods of time as mortality from cervical and leg fractures and hyperthermia are often the results (O'Gara and Yoakum, 2004).

Handling and Safety Considerations Most bovids and ungulates that weigh 60 to 70 kg or less can be physically restrained by a single person of medium build. Larger animals require additional personnel or individuals of large stature for safe physical restraint. Hobbles that are constructed of leather, canvas, or synthetic materials are very useful for safely restraining hooves and legs. Blindfolds are a necessary tool for animals that are to be physically restrained because they reduce stress (Fowler, 1995; Mitchell et al., 2004) and protect the eyes from damage. They can be made from a variety of materials but should be able to be removed quickly and should be comfortable for the animal.

Other safety items include foam and rubber balls or hose that can be placed on the sharp tips of horns to prevent injury to handlers for species such as mountain goat, bison (Bison bison), and musk oxen (Ovibos moschatos). Horns of young bovids and sheep are easily damaged during capture when nets are used because of slippage of horn sheaths that are loosely attached in younger animals. This can lead to moderate to severe blood loss, but long-term damage is usually not severe with the exception of disfigured horns for the remainder of the animal's life. Male cervids and caribou (Rangifer tarandus) and reindeer of both sexes should not be captured during the season of antler growth (May/June) if possible because of the high vascularity and potential for blood loss and associated pain when rapidly growing antler is damaged. Physical restraint and capture should be avoided on slippery surfaces such as ice and steep slopes because of the potential for injury.

In captive and semi-captive situations, artiodactylids can be easily and efficiently handled in specially designed handling facilities that include chutes, paddocks, and runs specifically designed for each species. The evolution of the game farming industry in North America has led to the development of sophisticated squeezes that use drop floors, padded sides, and hydraulics to minimize struggling and injury (Haigh, 1999). Individual animal habituation is an important prerequisite, if at all possible for successful physical restraint in these systems regardless of species (Grandin, 1993). Crash gates are an important component of bison handling systems that allow animals to be more easily restrained in a mechanical or hydraulic neck squeeze (Haigh, 1999). Holding pens and runs need to be designed with walls that are high enough to prevent escapes (10 feet or higher for sheep and goats) and designed to minimize injury to animals and humans during use. Points where animals are squeezed into narrow areas need particular attention to detail and specific flight distances of each species needs to be considered during design.

Captive artiodactylids can be habituated to routine handling procedures such as venipuncture, vaccination, and or physical examination with minimal restraint in a chute or box stall depending on individual animal temperament (Citino, 2003; Wirtu, 2005). The simplest systems use a circular or semi-circular tub with movable walls that squeeze the animal between them. It is important to have a large number of access panels to be able to gain access to all parts of the animal safely.

Well-designed box chutes have been successfully used for restraint of wild elk in Banff National Park for venipuncture, TB testing, and deworming and for wild bison and elk in Elk Island National Park in Canada for several decades (Figure 12.1).

Figure 12.1. Elk restrained in a chute.

Canidae/Felidae

Remote Capture Techniques Helicopter net gunning has proved to be a very successful method for capturing large carnivores in North America, especially grizzly (Ursus arctos), black bears (Ursus americanus), and wolves (Canis lupus). Wolves can be safely restrained after being netted using a forked stick or pole snare to pin the animal. Hobbles are useful to restrain the legs and nylon dog muzzles or duct tape can be used to restrain the mouth safely without chemical immobilization. Safe handling of bear species generally requires chemical immobilization after netting, with the net providing a quick way of immobilizing the animal so it does not injure itself in terrain with natural hazards (water, steep slopes). A common complication of net gunning large carnivores is the ability of the animal to chew its way out of entanglement; therefore, animals need to be either darted or restrained very quickly (within minutes) after the net is fired. Medium-sized canids such as covotes (Canis latrans) and wolves also have been captured very successfully with helicopter net gunning. Deep snow conditions are a definite advantage when attempting to capture canids using this method, as they are highly maneuverable on bare ground. Snowmobiles also have been used for capture of coyotes in winter in southern Canada by using a throw net in open, prairie environments (Moehrenschlager, 2000).

Various restraint traps designed to catch animals by a limb are used successfully to capture wolves, coyotes, foxes, procyonids, and some mustelids. The most widely used method of capture uses a modified foothold trap designed to minimize injury in captured animals (Sahr, Knowlton, and Frederick, 2000; Earle et al., 2003). These traps use padded jaws and laminated jaws to reduce potential for injury on the trapped limb (Figure 12.2).



Figure 12.2. Padded leg hold traps with laminated jaws can decrease the risk of injury to the trapped limb.

Swivels and drags are also important to ensure the trap does not get entangled and place additional rotational force on the trapped limb.

Other foothold traps include leg snares and are generally constructed of wire cable coated with protective coating and many are activated with a spring. Leg snares have been used for successfully capturing pumas (Felis concolor) (Logan et al., 1999; Logan and Sweanor, 2001), lions (Panthera leo) (Frank, Simpson, and Woodroffe, 2003), and Siberian tigers (Panthera tigris altaica) (Goodrich et al., 2001) and a modified snare within an oval-shaped container called an EGG (EGG Trap Company, Springfield, SD) trap has been widely used for capturing raccoons (Procyon lotor) and possums (Didelphis virginania) (Hubert et al., 1999; Austin et al., 2004) with minimal injury. Canada and the United States retain international agreements with the Russian Federation and the European Union to develop humane foothold traps for capture of fur-bearing animals in the fur trade that are scheduled to come into force in 2007 (Fur Institute of Canada, 2005). These traps have been tested to ensure they are humane and cause minimal injury to trapped animals. Frequent trap checking is critical (minimum every 24 hours) to prevent injury to trapped canids. When used in winter, limb ischemia and frostbite can occur as circulation is impaired in the trapped limb, so these type of traps should be used with caution at temperatures below 0°C. Tranquilizer tabs impregnated with propiopromazine or diazepam are a useful adjunct and have been used successfully to tranquilize and reduce injury in trapped wolves (Sahr, Knowlton, and Frederick, 2000) and coyotes captured in neck snares. Most wild canids up to 60 kg in size can be safely restrained without chemical immobilization for short procedures, such as application of radio collars and venipuncture. Longer or more invasive procedures such as tooth removal or implant surgery require chemical immobilization.

Various commercially available and home-made cage or box traps constructed of wire and plastic mesh or completely enclosed wooden or metal boxes are used for capture of procyonids, small and medium-sized canids, and most felid species (de Wet, 1993; Wilson, 1996; Mudappa and Chellam, 2001; Harrison, Barr, and Dragoo, 2002; Grassman et al., 2004). Animals are baited into the trap that is triggered by a floor plate with a vertical guillotine or hinged door that closes when the animal is inside. Animals can then be hand injected or injected with a pole syringe if chemical immobilization is required. Physical restraint using a snare pole or gloves can be used on smaller species or for restraint of a limb or the muzzle. Extreme care must be exercised with the use of a snare pole when used over the thoracic area. Ensuring that a front limb is ensnared along with the neck or thorax for very short periods of restraint help prevent asphyxia from thoracic compression. Box traps and cages provide the advantage of providing security

and safety from predation or attack while the animal is trapped, unlike other restraint devices such as foothold traps, although they are not as portable.

Regardless of trap type being used, the frequency of trap checking needs to be 12 to 24 hours or less for most species. The potential for self-injury, hypothermia, dehydration, frostbite, and other complications is much higher the longer the animal remains restrained or trapped (Cattet et al., 2003). More frequent trap checks are desirable if possible in terrain that is easily accessible. A variety of trap monitoring devices such as VHF trap transmitters have been developed to increase the frequency of trap checking in more remote areas.

Neck snares with stops have been successfully used for capture of coyotes in North America offering an alternative capture technique in areas where foothold traps or box traps are ineffective or prohibited. Tranquilizer tabs are a useful adjunct to help prevent injuries from struggling in a neck snare. Circumference of the neck snare is of critical importance to prevent nontarget captures and to decrease the potential for injury and mortality.

Felid species that utilize trees for safety and cover such as puma, jaguar, panthers (Felis spp.), bobcat (Lynx rufus), and lynx (Lynx Canadensis) can be captured with the use of trained tracking hounds (Apps, 1996, 1999; Taylor et al., 1998; Deem, 2004). Treed felids are generally chemically immobilized with a variety of remote drug delivery techniques, including blowpipes, pole syringes, dart pistols, and rifles. Injuries occur when dogs attack immobilized animals and when immobilized animals fall from heights greater than 5 meters. These are prevented by securely tying up dogs prior to darting and using nets, slings, or inflatable devices to cushion falls. Drug dosage can be a critical factor when chemically immobilizing large felids in trees and needs to be considered when choosing an appropriate drug combination (Beier et al., 2003).

Captive felids are generally captured or restrained with hoop nets, squeeze cages, or chemical immobilization depending on their size. Felid species less than 14 kg can be safely handled with a net and gloves (Fowler, 1995), whereas larger felids require specialized squeeze crates or snare poles for safe handling. Previous habituation and acclimation to handling facilities is extremely helpful in handling large felids without chemical immobilization for venipuncture and vaccinations.

Handling and Safety Considerations Heavy leather gloves are very useful when handling infant large felids or medium-sized felids as their teeth and claws can inflict serious damage to anyone holding them. Bacterial infections are common sequelae to felid and canid bite wounds, and all bite wounds should be considered contaminated and treated appropriately (Brook, 2005). Restraint bags designed for domestic cat restraint are useful for restraint of small and medium-sized cats



Figure 12.3. Muzzles and hobbles should be used with physically restrained canids to decrease the risk of injury to handlers.

for very short procedures such as venipuncture, injection, or vaccination, whereas hobbles and blindfolds are often used for larger canids.

Firearm backup is recommended for the larger felids when immobilized in case of spontaneous arousal. Snare poles are useful to restrain the feet of large felids when immobilized as a backup restraint mechanism or strapping them to a table or other flat surface when anesthetized. Small and medium-sized canids can be restrained by hand easily if the feet and muzzle are adequately restrained (Figure 12.3).

Ursidae

Remote Capture Techniques Aldrich leg snares have been used as a primary means of capture for various ursid species around the world for both research and management purposes for decades. They have the advantage of being portable, highly efficient, and easy to set in remote locations. The basic design involves a braided steel cable that forms a loop and is activated by a spring steel throwing arm (Jonkel, 1993) that captures the bear above the carpal joint. These devices are usually anchored to a large tree and set in a hollowed-out area in the ground. Injuries are often sustained in leg snares from biting or chewing on digits, fractured limbs, muscle damage, distal limb edema caused by impaired circulation, and cuts and abrasions at the site of contact with the snare cable. Although very uncommon, intraspecific predation also has occurred with the use of these devices for capture of grizzly bears in Canada (Gibeau and Stevens, 2002).

Culvert traps are a variation of a box or cage trap on a larger scale and specifically designed for ursids. They were originally made from culverts used for road construction and are manufactured in a wide variety of designs. They have the advantage of protecting the trapped bear from the elements and predators. They have the disadvantage of being quite large and unwieldy and are generally only used in road accessible areas, although some are designed specifically for use in remote areas and delivered by helicopter. They are used routinely for management of problem black and grizzly bears throughout North America (Jonkel, 1993) and for research on Malayan sun bears (Te Wong, Servheen, and Ambu, 2004). They are also useful for recovering immobilized bears and for transporting them once they are recovered. Injuries primarily occur in the oral cavity (lacerations, broken teeth) because of chewing on mesh or openings in the trap designed for accessing the animal. Mortalities are very rare but can occur when multiple animals are trapped or animals sustain trauma from falling guillotine doors.

In captive situations, bears are usually isolated individually in separate pens or enclosures prior to chemical immobilization. Sows with dependent cubs may or may not be separated prior to immobilization of the sow, depending on the stress level of the individual. Most bears with the exception of cubs less than 25 kg need to be chemically immobilized to be handled safely. Cubs can be physically restrained or captured with nets or blankets. Climbing gear may be necessary to retrieve cubs of certain species such as black bears, which routinely climb trees to escape.

Handling and Safety Considerations For safety considerations, it is good practice to have an armed guard equipped with a firearm when capturing and immobilizing adult bears. This is not to protect against the immobilized bear recovering spontaneously, but to protect the immobilization team from other bears, which are often attracted to the site. Personnel need to be trained in firearm use and must be prepared to use lethal force if necessary.

Hobbles should be applied to the limbs of immobilized bears to restrict mobility if the animal should spontaneously arouse. Equipment and pharmaceuticals to deal with injuries sustained from capture (antibiotics, wound dressings, antiseptic agents) should be carried in the field when capturing wild bears.

Mustelidae, Procyonidae, and Viverridae

Remote Capture Techniques Small and medium-sized mustelid species fisher (Martes pennanti), marten (Martes americana), mink (Mustela vison), and weasels (Mustela spp.) can be physically restrained for short procedures using a cone-shaped cotton or mesh bag, which

can be used to restrain an animal for examination once it has been captured in a box trap or other device. A method for physical restraint of mink with gloves is described by Fowler (1995), which can be modified for fisher, marten, river otter (Lontra Canadensis), and small raccoons. Squeeze cages are also useful for mustelids to provide a method of quick restraint for intramuscular injections such as vaccination or injection of chemical immobilization drugs. Cage traps, box traps, and padded foothold traps are most commonly used for capture of wild mustelids and viverrids (Hubert et al., 1996). Hancock traps also have been widely used for capture of river otters, although they are not as portable as other trap types and tooth damage is frequent. Hoop nets work very well for initial capture of captive mustelids and viverrids in zoos followed by physical restraint with gloves or chemical immobilization.

Home-made box traps made from locally available timber have been used for wolverine (Gulo gulo) capture in North America because of the large home ranges and remoteness of habitat (Copeland et al., 1995). Trapped animals are then chemically immobilized with pole syringes or dart pistols. A flashlight is required to visualize the animal, as these traps are usually quite dark inside.

Skunks (Mephitis mephitis) present a formidable challenge if physical restraint is used alone because of their defensive use of spraying musk from their anal sacs when threatened. For this reason, chemical immobilization is always preferred unless extraordinary precautions are taken to prevent contact with the musk (safety glasses, protective clothing).

Handling and Safety Considerations Heavy or medium-weight leather gloves are a necessity for handling most medium and large mustelids and viverrids owing to their extremely sharp teeth and propensity for biting when threatened. Most species can be handled by grasping firmly around the base of the head with one hand and the tail with the other hand (Fowler, 1995), but a sturdy grip is required due to their extreme flexibility and maneuverability.

Most mustelid species are very susceptible to stress especially when wild animals are held in captivity (Hartup et al., 1999; Fernandez-Moran, Saavedra, and Manteca-Vilanova, 2003) for a period of time. Skunks, bats, foxes, and raccoons are considered natural reservoirs of rabies virus in North America, so care should be taken to ensure personnel working with these species are vaccinated and trained to avoid exposure. Parasitic zoonoses such as Bayliscaris spp. cause severe neurological disease in humans and are also very prevalent in wild mustelids (Kazacos and Boyce, 1989) so care should be taken to avoid exposure to feces.

Rodents and Lagormorphs

Remote Capture Techniques Various cage and box traps are widely used for live capture of rodents and

lagomorphs. Small wild rodents less than 1 kg, such as mice, voles (Muridae), and ground squirrels (Sciuridae) are typically live trapped in either wire cage traps or metal box traps (Sherman traps) as part of ecological research studies or for pest removal. Specialized protective gear is required for handling certain species of small mammals that carry zoonoses, such as Hantavirus and tularemia (see Handling and Safety Considerations). Sherman traps are small aluminum box traps that are widely used for capturing small wild rodent species. Insulated bedding in the form of cotton or polyester fiberfill and a food source is required for microtine rodents because of their propensity to develop hypothermia and hypoglycemia (Jones et al., 1996).

Wild lagomorphs are generally trapped in wire cage traps baited with food. Injuries to teeth result from chewing on wire, so wood or plastic boxes with solid sides have been used to prevent this (Sharp and Saunders, 2004). Lagomorphs, especially snowshoe hare, are prone to hypoglycemia (trap sickness) if trapped in box or cage traps; therefore, a source of food should be provided or traps should be checked frequently (Feldhamer, Thompson, and Chapman, 2003).

Aquatic rodents such as beaver, muskrat, and nutria can be captured in specialized hinged cage traps called Hancock or Bailey traps or wire cage traps set on land (Rosell and Kvinlaug, 1998). Care must be taken to prevent traps from tumbling into water and drowning animals. These species can be netted from boats or chased from lodges and houses also (Rosell and Hovde, 2001) into nets.

Pit traps are occasionally used in conjunction with drift fencing for small microtine rodent capture by burying a round metal or PVC container which is 20 to 40 cm in diameter in the ground 40 to 50 cm deep (Jones et al., 1996).

Handling and Safety Considerations Mice and ratsized rodents can be handled with latex examination gloves by grasping the skin over the nape of the neck for short periods of restraint and non-invasive treatments. Larger rodents and lagomorphs require support if picked up or carried in this manner. Rats (Rattus spp.) and muskrats (Ondatra zibethica) are usually held by the tail with the feet allowed to grasp a surface such as a wire cage. Heavy leather gloves are required for larger species such as muskrat, beaver, and nutria to prevent injury to the handler from biting. Species with haired tails such as squirrels, marmots (Marmota spp.), and pack rats (Neotoma spp.) should not be restrained by the tail only as the hair and skin can easily slip causing severe injury (Fowler, 1995). Laboratory techniques that are well developed for mice, rats, guinea pigs, and hamsters often fail to restrain their wild counterparts unless personnel are very experienced in handling these species.

Medium-sized rodent such as hyrax, agoutis, marmots, and woodchucks can be netted and restrained manually for injections, quick examinations, venipuncture, and vaccinations. Specially designed squeeze cages that allow the animal to be forced against the side of wire cage or box are very useful for these rodent species.

Most lagomorphs can be manually restrained by grasping them around the base of the head with one hand and supporting the body and restraining the hind legs with the other hand. Severe spinal injuries can result if the hind legs of hares and rabbits are allowed to kick and flail while restrained. Gloves are important to prevent scratches and bites when handling larger hares and rabbits. Nets are useful for initially capturing lagomorphs in small enclosed spaces until they can be manually restrained.

Larger rodent species such as capybara (Hydrochoerus hydrochaeris) (Fowler, 1995), beaver (Castor Canadensis), and nutria can be netted and physically restrained for short periods for quick injections or vaccinations only. More invasive handling requires chemical immobilization. Beavers should not be hoisted by the tail alone, but can be restrained on the ground using the tail and a hand around the base of the head (Whitelow and Pengelley, 1954).

Porcupines (Erythizon dorsatum) are specialized rodents with various-sized quills that present a challenge for physical restraint. North American porcupines have barbed quills approximately 1 to 4 cm long, whereas Old porcupines such as crested porcupines (Hystrix spp.) have extremely long stout quills up to 45 cm long (Fowler, 1995) that are capable of severe injury. North American porcupines use their tail as a quill delivery system and contrary to popular belief, are incapable of "shooting" their quills. Sturdy plastic garbage pails or tubs with bottom cut out can be used to capture porcupines in small enclosures as nets often get entangled in the quills, where they can be chemically immobilized using a pole syringe or hand injection. Crested porcupines have particularly thin, fragile skin and are prone to injury and laceration from pole syringes (Fowler, 1995). Brooms or small plywood boards are useful to safely move porcupines into enclosures or transport containers although they often tend to go backward with quills flared rather than forward like most mammals.

Plexiglas or clear plastic induction chambers are very useful for induction of gas anesthesia in rodent species that are not easily handled or prone to injury such as porcupine and voles.

Zoonoses are a major concern with many species of wild and domestic rodents and suitable precautions need to be taken when handling them. Hantavirus is carried subclinically by several rodent species in North America including the white-footed deer mouse (Peromyscus maniculatus), cotton rat (Sigmodon hispidus), rice rat (Oryzomys palustris), and white-

footed mouse (Peromyscus leucopus). Prevalence varies dramatically with geographical location and year, and so the known carrier species should be considered infected at all times. Virus is shed primarily in saliva, urine, and feces, so examination gloves and HEPA filters should be worn to prevent transmission while handling. Plague (*Yersinia pestis*) is enzootic in prairie dogs in the American midwest and is carried by many other wild rodent species. Humans are generally infected through the bite of an infected flea from rodents or domestic cats that have been exposed to infected rodents and their fleas. Lyme disease caused by the spirochete *Borrelia burgdorferii s.s.* is carried primarily by Ixodes spp. ticks found on many rodent hosts, but particularly deer mice in eastern and midwest United States.

Monotremes and Marsupials

Handling and Safety Considerations Medium-sized marsupials with tails such as kangaroos and wallabies can be safely restrained for short procedures by grasping the animal by the tail and grasping the head with the other free hand to control head movement. This is most easily accomplished against a wall or other solid vertical surface. Large male adult kangaroos can be difficult to restrain and the hind feet are formidable weapons, so blankets or tarps can be used to initially tackle the animal and a minimum of two people are required. Koalas are captured by use of long snare poles or simply grabbed from branches of trees.

Primates

Medium-sized non-human primates (monkeys, vervets) are usually captured in box or cage traps or captured manually with long-handled nets. Larger ape species such as orangutan and gorillas require chemical immobilization using remote delivery techniques and are generally not physically restrained.

Handling and Safety Considerations Captive primates in the 3- to 12-kg range can be manually restrained by a person with heavy leather gloves by holding the front limbs and body in one hand and the hind limbs in the other hand. A face mask, shield, or safety glasses are also required for non-human primates because of the risk of zoonotic diseases (see below). Long-sleeved coveralls and leather gloves with sleeve extensions should also be considered to prevent bites and scratches. Most primates possess considerable strength and agility for their size, a fact often underestimated by inexperienced personnel.

Primates and great apes greater than 12 kg should be chemically immobilized unless extensive training and habituation to procedures has been completed previously. Many zoos and research centers train primates to present limbs through custom designed restraint cages and boxes for venipuncture, TB testing, vaccinations, and other minor procedures. Great apes

such as orangutans, gibbons, chimpanzees, and gorillas generally require chemical immobilization for safe restraint unless extensive training has been completed. Commercial squeeze cages are available for most species, which facilitate short procedures such as injections and visual examination of TB testing.

When any physical restraint of primate species is going to be necessary, appropriate safety measures should be in place to ensure protection from zoonoses. Herpes B virus causes a fatal encephalitis in humans and is carried by macaque (Macaca spp.) species (Johnson-Delaney, 2005). Primate keepers and any staff coming in contact with fecal material or urine need to wear masks, eye protection, and latex gloves as a minimum to prevent exposure when handling animals and when cleaning enclosures. Other potential zoonoses include hepatitis, HIV, Ebola viruses, and many others. The potential for reverse zoonoses should also be considered when handling primates and measures to prevent sick humans from coming in contact with primates should also be considered. Bite wounds also can be quite severe causing severe pyoderma and fasciitis.

Bats

Remote Capture Techniques Mist nets strung in various configurations, heights, and lengths are a versatile, portable, and inexpensive way to capture most bat species. Their use is limited at roost sites where numerous bats could be potentially captured as bats need to be untangled from the net, usually allowing the capture of single bats. Mist nets can be constructed of monofilament nylon, braided nylon, or braided Dacron polyester (Kunz, Tidemann, and Richards, 1996) and set up in numerous configurations wherever bats are found. Care must be taken when extracting bats from mist nets as their delicate wing bones and membranes are easily damaged. Wearing light leather gloves and allowing the bat to bite and hang on is often helpful to allow extraction (Kunz, Tidemann, and Richards, 1996).

Harp traps and Tuttle traps consist of vertical wire strands attached to springs within a rectangular frame that has a cloth or burlap bag attached to the bottom to catch bats that fly into the wires. Larger versions of this trap have been successfully used to capture megachiropteran bat species as well (Tidemann and Loughland, 1993). These traps are very useful for capturing bats at roost sites also.

Handling and Safety Considerations Small bat species (less than 100 g) can be held in the palm of the hand firmly but gently in a manner as described for passerine birds, with the thumb and index finger restraining the head. Larger megachiropterans require two hands to restrain the wings and head effectively. Open-weave cloth or mesh bags with drawstring tops are useful for temporary holding or transport of bats. Physical restraint should be minimized in most bat species, as hyperthermia

results from excessive struggling and stress (Heard, 2003). Light leather gloves such as golf gloves are used for handling microchiropteran species, whereas heavier leather gloves should be used for large pteropid bats.

Injuries to bats can be sustained to patagia, wing bones, and leg bones from improper restraint and attempting to dislodge bats from wire and net surfaces too forcefully (Heard, 1999). Personnel working with bats must be vaccinated against rabies, as most species are potential carriers of rabies virus or other lyssaviruses (Heard, 2003). Other viruses with zoonotic potential are also carried by bats, including Hendra, Nipah, Menangle, and Tioman viruses, which are carried by bats in Southeast Asia and Australia (Krauss et al., 2003). An important fungal disease, *Histoplasma capsulatum* has been linked to aerosol inhalation of bat guano in roosting caves, so masks with HEPA filters are recommended when working in caves where bats roost (Huhn et al., 2005).

Suidae, Tapiridae, and Tayassuidae

Remote Capture Techniques Tapirs (Tapirus spp.) in captive facilities are generally quite docile and many procedures can be accomplished with the animal standing or gently rubbed down and put in an almost hypnotic state. Foot trims, detailed examinations, TB testing, radiographs, and venipuncture can often be performed if animals are trained and habituated to these procedures. Tapirs are generally either rubbed along the sides or back with a comb or a gloved hand, which causes them to lie down in ventral or lateral recumbency. If animals cannot be trained to this procedure, chemical immobilization is required. Tapirs can also be gently herded with brooms or boards into squeezes and crates for treatment or injection.

Wild and exotic suid species such as warthogs (Phacochoerus spp.), red river hogs (Potamochoerus porcus), babirusa (Babyrousa babyrussa), and collared peccaries (Tayassu tajacu) can be physically restrained and captured using many of the same techniques used for domestic pigs, including snare poles and ropes, but they are much more difficult to restrain on a kg/kg basis. Most species have extremely sharp teeth and tusks and are capable of causing significant injury or death to people attempting to restrain them. Peccaries and smallsized pig species (less than 20 kg) can be caught with nets and restrained by stretching them out on a floor or mat by grasping the hind legs and head with gloved hands (Fowler, 1995). Adult pigs, warthogs, and babirusa must be either chemically immobilized or run through chutes and trained through operant conditioning to accept procedures such as vaccination and treatment (Morris and Shima, 2003).

Camelidae and Giraffidae

Members of this group of wildlife require special handling and restraint procedures which are well described elsewhere (Fowler, 1995, 1998, 2003; Bush, 2003).

Elephants

Specialized facilities are required to house and allow proper physical restraint of elephants in captivity (http://www.elephantcare.org/protodoc_files/azaele.pdf). Capture of wild elephants generally involves chemical immobilization using remote drug delivery techniques. Further information can be found at the following site (http://www.elephantcare.org/Elebase/ anesthes.htm).

BIRDS

Ratites

Most large ratite species such as adult ostrich can be physically restrained safely and easily for many procedures using custom-fitted hoods and appropriate handling facilities, which include triangular stocks, chutes, and boards to herd birds safely. Male ostrich are particularly aggressive during the breeding season and caution should be used when physically restraining an adult male ostrich. Ratites defend themselves with their powerful legs, which can strike out very quickly in a forward direction. Juvenile ratites can be easily restrained by grasping them from behind around the sternum and holding them with the legs dangling. The legs of juvenile ratites are prone to injury and should not be forced into position, but allowed to dangle freely. Once hooded, ostrich are easily restrained or walked short distances into a corner, where venipuncture, physical examinations, radiographs, ultrasound, and other husbandry procedures can be performed. The head of ostriches can be grasped and pulled toward to the ground to limit the risk of kicking out. Smaller ratite species such as emu and rhea also can be physically restrained by walking up to the bird and grabbing it from behind with both hands at the base of the wings and restraining the bird either standing or on the ground. Hoods are not applied to emus and rhea, as they often become more agitated when hooded. Doing this in a darkened room with solid walls and soft flooring helps avoid injuries. Cassowaries are an exception and chemical immobilization is usually recommended for these birds because of their aggressive nature and ability to seriously injure and kill humans with their sharp and powerful claws. Juvenile cassowaries can be safely physically restrained as described for rheas and emus.

Waterfowl (Anatidae) and Wading Birds (Herons, Cranes, and Storks)

Remote Capture Techniques Remote capture of water-fowl is well described elsewhere (Bub, 1991; Bookhout, 1994) and consists of using rocket nets, hand nets, nets strung across waterways, and cage traps of various sorts. Capture of wild waterfowl species is often timed to coincide with molting as capture is made easier by the fact that birds cannot fly for a period of several weeks. Appropriate-sized nets can be used to capture birds in enclosures or aviaries, where they can be physically

restrained for most procedures. Bites can be inflicted on handlers from larger goose and swan species. Injuries to birds are often inflicted on carpi and feet from being crowded into areas with concrete or other hard surfaces, so rubber flooring or mats on walls are often used to decrease injuries in these areas.

Wading birds such as cranes, storks, and herons can inflict serious eye damage with their sharp, pointed beaks, so safety glasses or face shields are definitely required. These birds are generally herded gently with brooms or boards into corners where they can be grasped by the head and body. The bird is generally held with one arm around the body to restrain the wings and support the body while the other hand restrains the head and neck. The legs are restrained proximal to the hocks only as fractures, and capture myopathy result from struggling when attempts are made to restrain the legs more distally (Swenger and Carpenter, 1996).

Galliforms (Pheasant, Grouse, and Partridge)

Pheasant, grouse, partridge, and ptarmigan species are fairly easily handled with light gloves to protect from spurs and bites in larger species. Hoop nets are widely used in zoos for capturing these species, which are usually found on the ground. Some male pheasants have sharp spurs that can inflict injury to handlers, and the males can be aggressive during the breeding season. These birds are restrained by holding the bird next to the body, thus restraining the wings between the arm and body with the other hand restraining the legs. The head does not usually need to be restrained as these species rarely peck once restrained (Fowler, 1995).

Wild galliforms are generally trapped in box traps baited with grain or other feedstuff or with mist nets or hoop nets (Skinner et al., 1998; Mahan et al., 2002). Cloth or mesh bags are very useful for holding individual birds for short periods of time or for transport. Birds settle down considerably if kept in a dark area rather than in bright light. Cardboard boxes are also useful for transport of groups of birds. Capture myopathy and trauma are the main injuries sustained from trapping of wild galliforms (Spraker, Adrian, and Lance, 1987; Nicholson et al., 2000).

Hawks, Owls, and Falcons

Most raptor species can be physically restrained if the talons and wings are restrained adequately to prevent injury to themselves and the handler. Their extremely sharp talons are the main defensive weapon to be avoided when physical restraint is required. Nets are useful to initially capture fully flighted birds in aviaries or pens in appropriately sized nets that will capture the bird without injury.

Hawk species are best restrained with leather gloves by grasping the talons quickly and deftly with one hand with the palm facing toward the chest of the bird. The



Figure 12.4. Appropriate protective equipment and handling techniques decrease the risk of injury during restraint of birds of prey.

bird can then be dangled upside down until the wings and head can be grasped. These birds are best held against the chest or side with the wings folded and head facing toward the back of the person. Stockinette or mesh bags are useful to restrain birds temporarily for weighing and venipuncture, banding, or radiographs without the need to hold them. Care needs to be taken to ensure that chest excursions are not restricted when using any physical restraint technique with avian species. The beak also needs to be avoided, as painful injuries can be sustained by large hawks, eagles, and owls (Figure 12.4).

Wild hawks and owls are captured by a variety of methods, including box traps, nets, and leg snares (Bub, 1991). Eagles are captured by chasing with vehicles (Ostrowski, Fromont, and Meyburg, 2001), on nests, or with snares (Hollamby et al., 2004).

Passerines

Remote Capture Techniques Nylon mist nets are the primary method of capture used for free-ranging and captive passerines in large aviaries. Passerine species include the thrushes, sparrows, finches, and others. Many methods of setting these nets have been described depending on the target species and its preferred habitat (arboreal, ground, or wetland). Most species can be held using a bander's hold in which the palm of the hand is used to gently cup the body to restrain the wings with the head being restrained between the index and middle fingers (Massey, 1999). Many of these species need to be handled as little as possible as they are prone to exertional shock and hypoxia from being over-restrained and not allowing the sternum to lift to allow air exchange in the lungs. The other method of restraint is to hold them in one hand by grasping the legs gently proximal to the hock joints with the index finger between the legs and the thumb and ring finger on either side. This works well if the birds are not flapping and struggling to escape or there is a need to transfer the bird from one person to another. Passerine species should be transported in dark containers or boxes to reduce flapping and struggling and can be removed using a towel or net to initially capture and restrain the bird. Most passerine species have fragile leg bones and rapid metabolic rates; therefore, injury and mortalities often result from prolonged or rough handling.

Psittacines

Most psittacine species can be physically restrained for most basic procedures including venipuncture, beak trims, nail trims, and physical examinations. Large macaws and parrots often need to be anesthetized for a thorough and less stressful examination. Most captive psittacines can be captured from a perch using a net or towel, depending on their level of tameness. Once captured, they are removed from the towel or net by grasping the head and mandible between the fingers of one hand and grasping the feet and wing tips in the other hand. Placing the bird in dorsal recumbency on a table or with a pad or towel underneath facilitate restraint. Gloves may or may not be used for psittacine restraint based on the temperament and size of the bird being restrained. Care needs to be taken with larger species, as they can inflict serious injuries with their powerful beaks. Detailed restraint and examination techniques for psittacines can be found in Romagnano (1999) and Abou-Madi (2001). Smaller species can be restrained as described for passerine birds.

REPTILES

Lizards, Skinks, and Geckos

Lizard species can be safely restrained if the head and tail are adequately restrained to prevent injury to the handler and animal. Carnivorous lizards (e.g., monitors, tegus) can be particularly difficult to handle, whereas young green iguanas and geckos are fairly docile to handle. Lizard species should not be restrained solely by the tail as many species can shed their tail (autotomy), so additional support and restraint must be used for the head and body. Small lizard species can be restrained in one hand with the head between thumb and forefinger and the ring and little finder wrapped around the pelvis to restrain the body and tail (Divers, 1999). If possible, medium-sized lizards initially should be grabbed over the dorsal pelvic area and pinned against a table or other flat surface and then grabbed behind the head while grabbing the forelegs; then they can be either wrapped in a towel or held against the body. Towels or hoods placed over the head facilitate handling of larger lizards, providing a calming effect. Leather gloves are very useful for large iguanas and monitors to prevent bites



Figure 12.5. Towels or hoods placed over the head facilitate handling of larger lizards.

and scratches. Special precautions need to be taken to avoid the bite of poisonous species such as the Gila monster and Mexican beaded lizard (Figure 12.5).

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Section IV Invertebrate, Fish, Amphibian, and Reptile Anesthesia

13

Invertebrates

Cornelia Gunkel and Gregory A. Lewbart

INTRODUCTION

What sort of topic is invertebrate anesthesia and analgesia? A better first question might be, "What exactly are invertebrates?" The invertebrates are a collection of animals, comprising more than 95% of the earth's species, unified by the lack of a vertebral column. Barnes and Ruppert (1994) stated that the invertebrates are a group of unrelated taxa that share no universal "positive" traits.

Depending on the text or specialist(s), there are currently over 30 recognized phyla of invertebrates (not including the protozoans). Many of these phyla may be considered obscure, but for no better reason than they may contain few species, microscopic representatives, or have no obvious economic value. In reality, each phylum and its members are important to the diversity and survival of the planet, even if the group is only studied by a small number of scientists. Unfortunately, very little is known about the veterinary and more specifically anesthesia/analgesia aspects, of many of these taxa. Writing a comprehensive book chapter for all invertebrate phyla would be an inefficient task. Consequently, we have elected to include, at least in this chapter, the most economically important and visible metazoan taxonomic groups.

The science of taxonomy is a dynamic and at times controversial branch of biology. We have elected to use the taxonomic terminology currently described in Ruppert, Fox, and Barnes (2004), with the knowledge that some invertebrate zoologists may use a slightly different nomenclature for some groups.

Invertebrate anesthesia is still in its infancy and very little research has been done to improve the understanding of the various anesthetic agents in this group of animals. The goal of this chapter is to provide an overview of anesthetic concerns and techniques in more commonly anesthetized invertebrates. It should be emphasized that more research is necessary to better understand and improve anesthesia in the different, and frequently unrelated, invertebrate species.

TAXONOMIC GROUPS

Mollusks

Anatomy, Physiology, and Natural History The mollusks are a diverse and large group of animals that occupy terrestrial, freshwater, and marine environments. There are probably about 100,000 described extant species in this huge phylum. Some are extremely important to the environment because of their ability to filter water and consume debris and detritus. Economically, they are one of the most important taxa on earth, and provide billions of dollars annually as a source of food, animals for pets, display, and research, and as jewelry, artwork, and the lucrative shell-collecting hobby.

Details of molluscan natural history, anatomy, and physiology can be found in a number of references, including Ruppert, Fox, and Barnes (2004), Lewbart (2006), and any general invertebrate zoology text. Malacology is the term used to describe the study of mollusks.

Despite their wide variety of function and form nearly all mollusks have the following common traits at some point in their life history: a muscular foot for locomotion, gills for respiration, a calcareous shell for protection and a mantle to secrete it, ciliated planktonic larvae for dispersal, and a chitinous radula for feeding.

We have elected to divide the mollusks into three groups. Only the most economically important classes are discussed, as these are the groups that have received some attention with regard to anesthesia and analgesia. Classes not covered include the Aplacophora, Monoplacophora, Polyplacophora (chitons), and Scaphopoda (tusk or tooth shells).

Gastropods

Anatomy, Physiology, and Natural History The gastropods are a large, important, and easily recognized group that includes the abalone, snails, nudibranchs, and sea hares. Most are aquatic and have a well-developed head with eyes and other sensory organs, an external shell,

muscular foot, and gills within a chamber for respiration. There are many exceptions, however, and one need only examine a common garden slug (no shell or gills and terrestrial) to appreciate the exceptions and diversity within the taxon.

Physical Restraint Gastropods are generally slow moving and easy to restrain manually or with a protective container. Although most gastropods are harmless to humans, members of the tropical genus *Conus* can inflict serious injury or even death with small toxic harpoons, which are modified teeth from the radula (Cruz and White, 1995).

Anesthetic Agents Used and Techniques Snails can be anesthetized with menthol or 5% ethanol (Flores, Salas, and Vedra, 1982) or inhalant agents like isoflurane (Girdlestone, Cruickshank, and Winlow, 1989). A commercial 10% Listerine® solution (ethanol 21.9%, menthol 0.042%) in normal *Lymnaea* saline is commonly used to anesthetize snails in research settings (Woodall et al., 2003). Sodium pentobarbital (0.4 mg/ml in water) has been reported with a very slow onset (8 hours), but good effect and low mortality rate (Martins-Sousa et al., 2001).

Isoflurane administration in terrestrial snails requires an anesthetic chamber with the ability for fresh gas inflow and waste gas scavenging (Girdlestone, Cruickshank, and Winlow, 1989). The MAC of isoflurane in the pondsnail is reported as 1.09 (Girdlestone, Cruickshank, and Winlow, 1989). Induction is fast (less than 10 minutes), but an excitatory period is common. One disadvantage is the need to take the animal out of the chamber for the procedure, which results in fluctuation of anesthetic depth and increased pollution. Furthermore, the depth of anesthesia may not be adequate for surgery.

Anesthesia in snails is defined as when body and tentacle withdrawal response to gentle stimulation is absent. Reflex tentacle withdrawal under inhalantanesthesia suggests an insufficient depth for surgery (Girdlestone, Cruickshank, and Winlow, 1989).

Ketamine and propofol do not produce anesthesia and might even show an excitatory, not a depressant, effect (Woodall and McCrohan, 2000). Ketamine/xylazine combinations may be toxic (Martins-Sousa et al., 2001).

Sea snails are commonly anesthetized with intracoelomic administration of magnesium sulfate or magnesium chloride (Clark et al., 1996). Induction is fast (2 to 5 minutes) and smooth, leading to good muscle relaxation. Halothane and MS-222 seem to be ineffective (administered as immersion or intracoelomic) anesthetic agents in this species (Clark et al., 1996).

Abalone Abalones are commercially farmed and frequently require physical examination and sizing, pearl seeding, and removal from the tanks for maintenance

and harvesting (White, Hecht, and Potgieter, 1996). Removal of abalones from the substratum is often only possible with mechanical assistance owing to their ability to tightly adhere to the substratum. This forced removal may result in injury with slow recovery or even death. Therefore, a muscle relaxing or anesthetic agent may be necessary to avoid stress and mechanical injuries related to dislodging. Protocols used in abalones for removal include ethanol (3%), 2-phenoxyethanol (1 to 2 ml/L), benzocaine (100 mg/L), magnesium sulfate (2 to 24 g/100 ml), and sodium pentobarbital (1 ml/L) (Aquilina and Roberts, 2000; Edwards et al., 2000). Magnesium sulfate is administered in water (4 to 22 g/100 ml) with dosage ranges depending on size (higher doses for larger animals) (White, Hecht, and Potgieter, 1996). Induction time is fast (5 to 8 minutes) and recovery is uneventful (3 to 35 minutes, depending on dosage and anesthesia time). Phenoxyethanol (0.05 to 0.3 ml/100 ml) also shows a fast induction period (1 to 3 minutes) and a good recovery time (5 to 20 minutes) (White, Hecht, and Potgieter, 1996). Nembutal (sodium pentobarbital, 1 ml/L) produces good muscle relaxation with an induction time of 15 minutes and complete recovery (Aquilina and Roberts, 2000). Clove oil (0.5 to 1.5 ml/L) and propylene phenoxytol (2.5 ml/L) are not recommended since both can cause unacceptable high mortality (Aquilina and Roberts, 2000; Edwards et al., 2000). MS-222 (1 g/L) and benzocaine (0.1 g/l) are ineffective as muscle relaxants (Aquilina and Roberts, 2000). Both MS-222 and propylene phenoxytol cause major excitation at induction, resulting in copious mucus production and loss of pigment (Aquilina and Roberts, 2000).

Recovery from any anesthetic includes thorough washing of the abalone and exposure to fresh flowing seawater at their optimal temperature (18°C) until muscle strength returns.

Cephalopods

Anatomy, Physiology, and Natural History This group of predatory and specialized mollusks includes such familiar forms as the squids, cuttlefish, octopuses, and the chambered nautilus. Most of these animals are pelagic and have the ability for fast locomotion. They have closed circulatory systems, high metabolic rates, and advanced nervous systems that include excellent vision and tactile senses. Most have an internal skeleton (shell) with the exceptions being the octopuses (no shell) and the nautilus (external shell). Other interesting features of most members include the ability to "ink" when disturbed or threatened, suction-cup discs on the arms, and internal fertilization. All of the approximately 700 extant species are marine.

Physical Restraint Generally these animals are difficult to handle, other than for a quick move or relocation,

without sedation. Buckets, plastic nets, or other objects may be used to capture or restrain cephalopods.

Anesthetic Agents Used and Techniques Ideally cephalopods should be anesthetized in their own seawater to maintain mineral balance. The two most commonly used anesthetic agents are magnesium chloride (MgCl₂) and ethanol. Cuttlefish have been successfully anesthetized with 1.5% to 3% ethanol (15 to 30 ml/L) diluted in seawater (Harms et al., 2006). Inductions are rapid (1 minute), especially at higher dosages, and dilution to a lower concentration (10 to 15 ml/L) to decrease the risk of overdosing should be considered. Transient excitement occasionally has been noticed during induction with lower ethanol concentrations (Harms et al., 2006). If the procedure cannot be performed in the water, anesthesia is maintained with a recirculating system (Lewbart and Harms, 1999) (Figure 13.1). The anesthetic concentration of the water is adjusted over time to the depth of anesthesia desired.

If magnesium chloride (MgCl₂) is used in cuttlefish, a 7.5% stock solution is prepared with distilled water (Scimeca and Forsythe, 1999; Gore et al., 2005). This stock solution is mixed with a known amount of seawater to prepare an anesthetic concentration suitable for induction. A final concentration of 6.8 g/L (100 ml of the stock solution mixed with 1 liter of seawater) has been reported to have an induction time of 6 to 12 minutes without side effects (Gore et al., 2005). Because of the size of the cuttlefish a total water volume of 6 to 8 liters is commonly needed. Induction is usually smooth and without a period of excitation. Decreases in concentration via dilution may be necessary over time to adjust anesthetic depth.



Figure 13.1. A recirculating anesthesia system containing dilute ethanol with an anesthetized cuttlefish (Sepia officinalis). Note that two irrigating tubes are being used, one for each set of gills. (Photo courtesy of J. Bolynn.)

Octopuses are an esthetized in a similar manner. Two commonly employed an esthetic agents are ethanol and MgCl₂. Ethanol (2% v/v in sea water) can produce excitement during the short induction time (tachypnea, at tempts to climb out of the solution, and ink ejection) (Andrews and Tansey, 1981). Induction time has been reported to be 4 minutes and time to full recovery as 2.5 minutes (Andrews and Tansey, 1981). Ethanol (2%) is not effective in cold water species (below 15°C) (Gleadall, personal communication, 2006).

Magnesium chloride is the preferred anesthetic agent in cephalopods. It is used by preparing an isotonic solution of 7.5% MgCl₂.6H₂O (in distilled water) mixed with an equal volume of seawater (Messenger, Nixon, and Ryan, 1985; Scimeca and Forsythe, 1999). Induction time lies between 1.5 and 13 minutes with a short period of hyperventilation, then a gradual increase in arm flaccidity and righting reflexes; it is considered to be very smooth (Messenger, Nixon, and Ryan, 1985; Culloty and Mulcahy, 1992). Respiration will decrease and even cease if the anesthetic concentration is not decreased. The gills should be intermittently or constantly perfused with anesthetic seawater. Time of recovery from MgCl₂ is fairly quick (1 to 10 minutes), but dependent on length and type of procedure (up to 20 minutes after longer procedures).

Controversial opinions have been expressed about the ability of magnesium chloride to produce adequate sedation and analgesia via blocking nerve transmission and neurotransmitter release, or acting only as a neuromuscular blocking agent (Clark et al., 1996). Differences in vertebrate versus invertebrate anatomy/physiology as well as routes of administration seem to play a role in the effects, but the issue remains unresolved (Clark et al., 1996). An analgesic should be added to the protocol for any painful procedure to assure adequate patient care.

The use of urethane has been reported (Andrews and Tansey, 1981; Messenger, Nixon, and Ryan, 1985; Gleadall, 1991) and was routinely used in the 1970s and 1980s. Despite good anesthetic effect, the traumatic effects on the animals are severe (excitement during the induction phase). Chloroform, chloral hydrate, and CO₂ are unsuitable anesthetic agents in cephalopods as they can cause high mortality (Gleadall, 1991; Garcia-Franco, 1992).

Hypothermia, despite its popularity in the literature, is not an adequate anesthetic and should not be used in this group of animals because of its lack of analgesic and muscle relaxing properties. Mortalities and distress have been reported (Bower et al., 1999). The underestimation of cardiovascular and respiratory system compromise during hypothermia, as well as in the phase of warming, may be one of the leading causes.

For recovery, the cephalopod is placed in a container with anesthesia-free seawater. Ideally the water is circulated and aerated. If spontaneous respiration is not

present, gentle and slow mantle massage can be used until normal respiration is restored. The tentacles remain extended and flaccid in the first phase of the recovery and will retract in response to light pinching with progressive awakening (Harms et al., 2006).

Resuscitation of cephalopods includes squeezing and relaxation of the whole mantle/body for water circulation over the gills and hemolymph through the body (Harms et al., 2006). Anesthesia-free water should be directed over the gills for a washout effect.

Cephalopods are commonly monitored with visualization of respiratory rate and pattern. Normal awake values for Octopus vulgaris in a weight range from 100 to 800 g is 26 to 30 breath/minutes (Andrews and Tansey, 1981). The cardiovascular system is assessed by placing a Doppler probe on the dorsal area (above the aorta) or behind the gills (above either branchial heart) to monitor heart rate and blood flow. A pulse oximeter will likely give false readings because of the presence of hemocyanin instead of hemoglobin, but may be used for heart rate. In transparent species (especially with MgCl₂), the pallial organs can be observed. Depth of anesthesia is difficult to assess in cephalopods. Level of anesthesia seems adequate when there is no response to tactile and surgical stimuli, contraction of the skin around the eye in response to pressure on the eyeball, or withdrawal of the animal in response to a pinch of the skin over the eye (Andrews and Tansey, 1981). Further indicators of anesthetic depth are the flaccidity of the arms, loss of normal posture, and inability to regain normal posture after disturbance (Andrews and Tansey, 1981). Respiration usually remains spontaneous; a depression or cessation is a sign of critical deep levels of anesthesia.

Bivalves

Anatomy, Physiology, and Natural History This large and economically important group of highly evolved mollusks includes the clams, mussels, oysters, and scallops. They lack a well-developed head, are generally nonvisual (the scallops are an exception), feed by filtration using the gills for food transport, and use a muscular and sometimes large foot for locomotion. All of the approximately 8,000 described extant species are aquatic and nearly 80% of these are marine.

Physical Restraint Most bivalves are easy to handle and restrain safely. Nearly all tightly close their calcareous valves when handled or disturbed and may require sedation or physical manipulation (prying) to open the valves, which are held fast by strong adductor muscles.

Anesthetic Agents Used and Techniques

Oysters Propylene phenoxetol is used as a 1% solution to anesthetize oysters in a dosage range from 1 to 3 ml/L. Higher dosages induce a rapid and relative deep level of anesthesia (Mills, Tlili, and Norton, 1997) and may need

decreasing throughout the procedure to minimize recovery time (Norton et al., 1996). Generally, concentrations of 1 to 2 ml/L are safe and effective. The oyster should be placed hinge down in the solution, leaning against the walls of the aerated container to facilitate monitoring. Induction time is reported to be between 6 and 15 minutes. Adequate anesthesia is reached when the oyster gapes wide enough to part the gill curtain inside the shell and shows no responsiveness to handling (Mills, Tlili, and Norton, 1997) or contraction of the tissue to a stimulus (Norton et al., 1996). A decrease in stress from handling before placing oysters into the anesthesia container will improve the anesthetic effects and opening. Recovery time is short (less than 30 minutes), although it depends on length of procedure, anesthetic concentration, and temperature (Norton et al., 1996). Recovery tanks should be aerated.

Magnesium chloride seems to have variable effects on oysters. Some describe little effect in pearl oysters (Norton et al., 1996; Mills, Tlili, and Norton, 1997), mainly owing to long induction times (1 to 2 hours). Culloty and Mulcahy (1992) reported good anesthetic effects, but also long induction and recovery times (90 minutes) at 3.5%. The effect of MgCl₂ seems dependent on species and concentration. MS-222 and chloral hydrate are not effective in oysters (slow induction and recovery) and are associated with complications including death. Some of these may be related to the low pH of unbuffered MS-222 (Norton et al., 1996).

Scallops Anesthesia may be required, but mainly for muscle relaxation. In general, the depth of anesthesia/ relaxation is adequate when handling and stimulating of the mantle tissue fails to stimulate shell closure. Recovery is often defined as the regained ability for shell closure in response to handling (Heasman, O'Connor, and Frazer, 1995).

Magnesium chloride is the drug of choice due to its rapid and consistent induction and recovery. The agent is pre-dissolved in seawater and then added to the aerated induction container to reach a concentration of 30 to 50 g/L. Induction times at these concentrations are quick and in the range of 2 to 6 minutes. Recovery time in scallops anesthetized with MgCl₂ seems to be consistently short (10 minutes) regardless of concentration used or temperature (Heasman, O'Connor, and Frazer, 1995).

Chloral hydrate seems to have variable effects in scallops with significant changes in induction and recovery at different concentrations and temperatures (Heasman, O'Connor, and Frazer, 1995). A concentration of 4 g/L produces anesthesia in about 10 to 25 minutes, if temperature is held at 24°C. Lower temperatures significantly slow induction. Higher concentrations shorten induction time, but can result in high mortality. Recovery time at 4 g/L is 20 to 30 minutes, but varies widely depending on temperature (and concentration).

Aerated recovery tanks and continuous flushing with seawater facilitate recovery.

Other drugs have been examined with little success. MS-222 induces hyperactivity and hyperextension, benzocaine causes an initial hyperactivity, metomidate results in shell-closure, ethanol does not seem to have any effect, and magnesium sulfate leads to high mortality (Heasman, O'Connor, and Frazer, 1995).

Giant Clams Giant clams (*Tridacna* sp.) have been anesthetized with propylene phenoxetol (Mills, Tlili, and Norton, 1997).

Arachnida

Introduction The arachnids are a large class of approximately 70,000 described species of terrestrial carnivores (Ruppert, Fox, and Barnes, 2004) chelicerates. All Chelicerata, a group that also includes the horseshoe crabs, scorpions, and sea spiders (Pycnogonida), belong to the phylum Arthropoda. Spiders, mites, and ticks make up the bulk of the arachnid species. Less conspicuous arachnids include the whip spiders, micro-whip spiders, harvestmen, pseudoscorpions, tick spiders, and sun spiders. Tarantulas (Mygalomorphae) represent an important group of commonly kept arachnids that frequently require medical care.

Spiders (Aranae)

Anatomy, Physiology, and Natural History The spiders comprise one of the largest orders in the class Arachnida (which belongs in the sub-phylum Chelicerata). There are approximately 40,000 described species (Araneae) belonging to 3,000 genera, with thousands more as yet undescribed (Ruppert, Fox, and Barnes, 2004).

Spiders range in size from a body of less than a millimeter to over 9 centimeters for large tropical tarantulas (Ruppert, Fox, and Barnes, 2004). The basic spider body plan includes two large segments, the cephalothorax and the abdomen, connected to each other by the pedicel. All spiders have four pairs of walking legs, paired chelicerae, and paired pedipalps. The fangs are located at the tip of the chelicerae and are used to immobilize prey, frequently by injecting venom. The male pedipalps are usually modified to aid in sperm delivery. The spinneret is located at the distal end of the abdomen and is used to spin silk, an ability that virtually all spiders possess and use for a variety of functions.

Spiders are carnivorous and perform most of their digestion outside of the gastrointestinal (GI) tract; food is digested in a cavity adjacent to the mouth and the liquefied food is then ingested. The GI tract is divided into the foregut (mouth, pharynx, esophagus), midgut (many branching cecae), and a short hindgut (Ruppert, Fox, and Barnes, 2004).

Spiders breathe through book lungs, trachea, or both. Tarantulas have two pairs of book lungs that are found on the ventral aspect of the abdomen. Most spiders have

just one pair of abdominal book lungs and a pair of tracheae. Other combinations and modifications on these two plans are found within the order (Ruppert, Fox, and Barnes, 2004).

Spiders possess an open circulatory system with the hemolymph functioning in oxygen transport, immune defense, waste removal, and limb mobility through hydrostatic pressure. The heart is large and located in the dorsal abdominal segment. Most spiders excrete uric acid as well as adenine and guanine as their nitrogenous waste products. Malpighian tubules absorb these compounds from the hemolymph and direct them into the cloacal chamber, where they are excreted with the feces (Ruppert, Fox, and Barnes, 2004).

Spiders have two main nerve centers located in the cephalothorax; the subesophageal and supraesophageal ganglia. Spiders sense their environment in a number of ways, including vision, tactile reception, chemoreception, and vibration detection. These are accomplished with four pairs of eyes, tactile hairs, chemosensory hairs, and slit sense organs respectively (Ruppert, Fox, and Barnes, 2004).

Sexes are separate in spiders and fertilization is generally internal. Female spiders produce egg sacs that may contain thousands of young and there are varying degrees of parental care among spiders. Although most spiders probably do not live longer than 2 years, some female tarantulas may live for several decades (Pizzi, 2006).

Physical Restraint Physical restraint is commonly used to handle and transport spiders (Figure 13.2). However, some tarantula species are capable of shedding urticating hairs that can be quite irritating, especially to individuals allergic to these structures. Other drawbacks to manual restraint are injury to the animal and potential envenomation of the handler (White, Cardosa, and Fan, 1995). It is advisable to wear latex gloves when handling spiders and to be cautious of dropping the spider or having it leap or fall to the ground.

Anesthetic Agents Used and Techniques Spiders are most commonly and successfully anesthetized with inhalant anesthetic agents. Many agents (halothane, isoflurane, sevoflurane, and desflurane) have been used. Of the potent inhalant anesthetics, halothane is least desirable for invertebrate anesthesia, because of the high likelihood of potential toxicity for personnel during gas delivery.

Several different induction chambers have been described (Cooper, 2001; Melidone and Mayer, 2005; Pizzi, 2006) and used successfully for delivering inhalant anesthesia to spiders. These chambers are either commercially available induction chambers (invertebrate-specific or regular small mammal induction chambers) with appropriate fresh gas inflow and scavenging outflow, or simple self-made clear plastic containers





Figure 13.2. A. Wearing latex gloves, or other protective measures, should be taken when handling many invertebrates, such as this rose hair tarantula (Grammostola rosea). **B.** Sensible physical capture and restraint are used to obtain a weight from this rose hair tarantula. (Photos courtesy of M. Mehalick.)

(Figure 13.3). Plastic containers without the use of an inflow and outflow system may be used by placing a cotton wool swab soaked with a small amount of inhalant agent into the box. The spider itself should be placed in a separate smaller container with small pores. The smaller container holding the spider is placed into the larger box. This allows the inhalant to diffuse into the box while ensuring that the spider cannot come into direct contact with the inhalant-soaked cotton swab. This method is not ideal because of the higher anesthetic exposure to personnel, less control of the amount of anesthetic given, and higher risk of overdose. Anesthetic gas given via a precision vaporizer is much preferred. The advantages of the chamber technique are convenience of use, low cost, and safety to the patient associated with the set up. The disadvantage is the animal can only be temporarily sedated or anesthetized. For any physical examination or surgery the animal is removed from the chamber, limiting the time for any procedure before the animal recovers. This may require repeated inductions, but also increases the exposure of



Figure 13.3. Inhalant anesthetic chamber for terrestrial invertebrates. Pictured here is an anesthetized rose hair tarantula (5% isoflurane). (Photo courtesy of M. Mehalick.)



Figure 13.4. Because the spider's respiratory intake is located in the abdominal segment, it appears that at least some species can be maintained on inhalant anesthesia, as shown here, whereas the limbs and cranial body parts are examined or manipulated. This is a rose hair tarantula (G. rosea). (Photo courtesy of M. Mehalick).

the clinician and staff to the anesthetic gases. A surgery chamber has been developed (Melidone and Mayer, 2005) that allows the clinician to perform the surgery or other manipulations on the animal without taking the animal out of the chamber.

Another interesting technique is to induce the spider in an anesthetic chamber and then place its abdomen (with the associated book lungs/tracheae) into a smaller chamber "sealed" with a latex glove (Figure 13.4). This technique appears to have some merit when a procedure must be performed on the cephalothorax or limbs (Dombrowski, 2006).

The most commonly used anesthetic agents for spiders are carbon dioxide, isoflurane, and sevoflurane (Cooper, 2001; Melidone and Mayer, 2005; Pizzi, 2006). The animal is placed into the chamber, which is then filled with the anesthetic gas in oxygen (about 3% to 5% for isoflurane; 4% to 6% for sevoflurane). To increase the

filling time in larger chambers the oxygen flow rate is high at the beginning (1 to 3 L/minute), but can be decreased to a minimum if there are no major leaks in the system (300 to 1,000 ml/minute). Oxygen flow lower than 200 ml/minute decreases the accuracy of the vaporizer and may decrease the amount of anesthetic agent in the chamber owing to the uptake of the animal. The amount of CO₂ in the chamber may also be increased using low fresh gas flows. An appropriate scavenging system is necessary to decrease pollution. With increasing depth of anesthesia the vaporizer can be adjusted (decreased over time). The MAC of the different anesthetic agents in spiders has not been determined.

Other agents, such as carbon dioxide (CO_2) and nitrogen (N_2) as well as hypothermia have been used to immobilize spiders (Madsen and Vollrath, 2000; Pizzi, 2006). No reports about the amount of nitrogen used or the quality of nitrogen anesthesia could be found. Carbon dioxide is administered as a gas in a chamber, often producing 98% saturation. Dilution with air or oxygen is hard to achieve, resulting in an increased risk for mortality (Pizzi, 2006). Hypothermia is not an anesthetic and does not provide analgesia. It is itself considered painful and should not be used as an anesthetic.

Observing the spider for righting reflexes and leg movements assists monitoring depth of anesthesia. During induction it may take 10 to 15 minutes with several attempts of the spider to move and reposition itself, until full immobilization has occurred. During the procedure leg movement in response to stimuli is an obvious sign of insufficient depth of anesthesia. A mild tachycardia and tachypnea may be seen, but is often unrecognized. A deep level of anesthesia is more difficult to evaluate and slow respiratory rate and low heart rates are often the only way to assess a patient for an excessive depth of anesthesia. An analgesic administered for painful stimulations may make it easier for the clinician to maintain a consistent level of anesthesia.

Respiratory rate is observed at the cranial lateral side of the animal. Often the heart rate can only be monitored in larger spiders. The heart lies under the dorsal surface of the body. With a Doppler (pinpoint-crystal head) placed over the heart area a rate can be obtained. Normal heart rates are considered to be 30 to 70 beats per minute in large spiders and up to 200 beats per minute in smaller species.

After turning off the inhalant and maintaining the animal on fresh oxygen flow or room air the recovery from anesthesia is gradual. It can take between 3 and 20 minutes depending on the ambient room temperature and the anesthetic depth during the procedure. Slow leg movements and righting attempts increase over time. When fully awake the animal is returned to its enclosure and maintained at its preferred ambient temperature. Feeding after anesthesia should be withheld for 48 hours (Pizzi, 2006).

Scorpions

Anatomy, Physiology, and Natural History There are about 1,200 species of scorpions. Most are nocturnal and found in warm climates such as the tropics and subtropics (Ruppert, Fox, and Barnes, 2004). They belong to the order Scorpiones and share many traits with their arachnid cousins, the spiders.

The basic anatomical plan consists of a cephalothorax, segmented abdomen, and telson, sometimes referred to as the sting (Ruppert, Fox, and Barnes, 2004). Although scorpions are infamous for their stinger and venom, a scorpion envenomation is rarely fatal to humans and normally induces only pain and discomfort (Dehesa-Davila, Alagon, and Possani, 1995). Scorpions can range in size from less than 10 mm to just over 20 cm.

Scorpions differ from spiders and most other arachnids in that they have a well-developed ventral nerve cord and exhibit viviparity with extended maternal care of the young in most species (Ruppert, Fox, and Barnes, 2004). For a more detailed account of scorpion anatomy, physiology, and natural history, please refer to Frye (2006) or Ruppert, Fox, and Barnes (2004).

Physical Restraint Direct handling should be kept to a minimum for both the safety of the handler and the animal. Clear plastic containers, and in some cases utensils such as long forceps, can be employed for moving an animal from one place to another (Frye, 2006).

Anesthetic Agents Used and Techniques Scorpions are anesthetized similarly to spiders (see preceding section). An induction chamber using anesthetic gas in oxygen given via a precision vaporizer is preferred. Isoflurane or sevoflurane can be used.

Crustaceans

Anatomy, Physiology, and Natural History The crustaceans are a large and diverse group of arthropods that are all aquatic at some stage of their life history. Some authors consider this group, with over 40,000 described species, a subphylum of the phylum Mandibulata (Ruppert, Fox, and Barnes, 2004). Other workers still consider it a class of mandibulate arthropods that have two pairs of antennae, biramous appendages, compound eyes, segmented excretory organs, a well-developed protective carapace, and an aquatic nauplius larva (Noga, Hancock, and Bullis, 2006). The majority of the most conspicuous and economically important crustaceans belong to the order Decapoda, which includes the crabs, crayfish, hermit crabs, lobsters, and shrimp.

Physical Restraint Some species can be manually restrained with gloved hands or in some cases with the help of utensils such as nets or tongs (Figure 13.5). Because some crustaceans such as lobsters and large crabs can cause serious injury to handlers, care should be taken when manipulating or restraining these animals.



Figure 13.5. This blue crab (Calinectes sapidus) is being manually restrained while hemolymph is collected. (Photo courtesy of M. Mehalick.)

Anesthetic Agents Used and Techniques Crustaceans can be anesthetized with various agents. Depending on the animal's size and procedure, MS-222, isobutyl alcohol, and intramuscular (IM) injections of lidocaine, ketamine, or xylazine have been reported (Oswald, 1977; Brown et al., 1996; Ferraro and Pressacco, 1996; Gardner, 1997). MS-222 is generally accepted as a non-effective agent to produce anesthesia in decapods (Oswald, 1977; Gardner, 1997) and only very high doses show some effect (greater than 1 g/L) with very slow induction time (Brown et al., 1996; Gardner, 1997).

Lidocaine (0.4 to 1 mg/g) can be injected IM into the tail and its effect lasts for 5 to 30 minutes in crayfish, depending on the dose administered, with an average induction time of 1.5 minutes (Brown et al., 1996).

Ketamine has been used in crayfish (40 to 90 µg/g), (Brown et al., 1996), and in the Australian giant crab (P. gigas) (0.025 to 0.1 mg/kg intravenously [IV]) (Gardner, 1997) with variable response. Ketamine IM in crayfish provides consistent anesthesia (induction time: 1 minute) for over 10 minutes (40 µg/g) to almost 2 hours (greater than 90 µg/g) without excitatory side effects during induction or recovery (Brown et al., 1996). When ketamine alone was given to the giant crab IV, a short period of excitement occurred, but induction time was fast (15 to 45 seconds) (Gardner, 1997). Duration of anesthesia was dose dependent and lasted between 8 and 40 minutes.

Xylazine has shown good anesthetic effects in adult giant crabs when used at doses between 16 and 22 mg/kg IV (Gardner, 1997) or in common shore crabs at 70 mg/kg IV (Oswald, 1977). Induction seems to be smooth and fairly fast (3 to 5 minutes) and immobilization lasts 25 to 45 minutes (depending on the dose administered). Side effects such as bradycardia, extrasystoles, and dysrhythmias have been reported with high dosages (70 mg/kg) (Oswald, 1977).

An IV injection can be preformed in adult giant crabs through the coxal arthropodal membrane of a cheliped

(Oswald, 1977; Gardner, 1997) using a small needle (25 gauge). The presumption is that drugs such as ketamine and xylazine also can be administered IM, although this may lead to a slightly longer induction time. No published research has been done in combining these drugs or the use of other anesthetic agents such as etomidate, metomidate, or propofol IV.

Procaine (25 mg/kg IV) also has been used in crabs and provides good anesthesia with a very short induction time (20 to 30 seconds). This included a 10-second-long excitatory phenomena that led to tonic contraction before paralysis. Duration was very long (2 to 3 hours) with slow recoveries (Oswald, 1977) and may be reserved for long-term experimental anesthesia.

For smaller crabs, in which an IV or IM injection is impractical, clove oil can be used as a bath treatment and has shown a 16-minute onset of anesthesia at a dose of greater than 0.125 ml/L and a long recovery phase (2.5 hours). Once the animal is anesthetized a reduction of concentration is necessary, because clove oil at 0.125 ml/L over a longer period of time is also used for euthanasia of these animals (Gardner, 1997).

Monitoring Crustacean heart rates can be measured by applying electrocardiograph pads with ample gel on the shell above the heart. The normal heart rate for lobsters is between five and 20 beats per minute, with a circadian influence (higher at night) (Aguzzi, Abello, and Depledge, 2004) and 30 to 70 beats per minute for the shore crab (Styrishave, Andersen, and Depledge, 2003), depending on pH and temperature. Depth is evaluated in crustaceans by the relaxation of the body and the ability to withdraw extremities and very slow withdrawal of their antennae.

Insects

Anatomy, Physiology, and Natural History The insects are an incredibly diverse and numerous group that some taxonomist term the Hexapoda. With nearly a million described species, they are the true taxonomic champion of sheer species numbers and diversity. Most species are terrestrial, some are aquatic, and the only habitat they have not exploited is the ocean (some are found in the intertidal zone). Insects are arthropods with three major body segments (head, thorax, and abdomen) and three pairs of legs. Most have keen eyesight, well-developed mouth parts, sensory antennae, and wings. They have an open circulatory system that contains hemolymph and gases are exchanged through spiracles that open into a system of tracheae. Most species lay eggs following internal fertilization.

Physical Restraint In most cases insects can be handled and restrained manually without risk to the animal or handler. In some cases gloves are recommended as a protective measure and various utensils can be employed to immobilize or restrain insects. Much

depends on the size and species of insect with which you are working.

Anesthetic Agents Used and Techniques Carbon dioxide remains a popular agent to immobilize insects in entomological research, although multiple side effects, including convulsion and excitation at induction, are well recognized and mortality is high (Nicolas and Sillans, 1989; Valles and Koehler, 1994). Its use remains controversial and a more progressive approach would be the use of a volatile anesthetic agent such as isoflurane or sevoflurane. This requires a chamber apparatus to allow for appropriate delivery and scavenging of the inhalant agent (Walcourt and Ide, 1998).

Echinoderms

Anatomy, Physiology, and Natural History The echinoderms are a diverse phylum of about 6,000 extant marine species in six classes that all share, at least at some point in their life history, pentamerous radial symmetry. Familiar members of this phylum include the sea lilies, feather stars, sea stars, brittle stars, sea urchins, sea biscuits, sand dollars, and sea cucumbers. Echinoderms have a water vascular system that is used for feeding, locomotion, and transport of coelomocytes used in the immune response. Nearly all species have a skeleton composed of calcareous ossicles and in some cases these ossicles are fused to form an external structure called the test (e.g., sea urchins). The nervous system is composed of a nerve ring with associated radial nerves (there are no ganglia). Fertilization is external and most species have planktonic larval forms.

Physical Restraint Many species can be readily handled safely and effectively without anesthesia or sedation. Most tend to be slow moving and quite hardy (one exception is the brittle stars). Certain species of sea urchins can inflict a painful sting with movable, sharp spines (Mebs, 1995). Nets, tongs, and gloves can aid in the safe handling of many species.

Anesthetic Agents Used and Techniques Echinoderms can be anesthetized/immobilized with MgCl₂, MS-222, or menthol (Harms, 2006). Ideally the sea star (starfish) is anesthetized in its own seawater (i.e., the water they are adapted to in their aquarium), to keep temperature and water content (including pH, salinity, etc.) consistent. To a known amount of that water, a MgCl₂ solution (7.5% to 8% in tap or seawater) is administered. A 1:1 mixture has been reported (McCurley and Kier, 1995), and may be necessary for induction, but adjustments over time during maintenance of anesthesia may have to be made (gradually administer more seawater). MS-222 can be used in a concentrated form (1 to 10 g/L in seawater) (O'Neill, 1994; Hendler et al., 1995). Other reported anesthetic agents are menthol (2.5% to 5% in sterile seawater) (Costello and Henley, 1971) and

propylene phenoxetol (2 ml/L in seawater) (Van den Spiegel and Jangoux, 1987; Hendler et al., 1995).

PAIN MANAGEMENT

Whether invertebrates feel pain is still an unanswered topic of debate (Chapter 3). The crux of the debate may lie in the differentiation between nociception and pain per se. Nociception describes the neurophysiological components leading to the sensation of pain but excludes the central perception of nociceptive input that ultimately leads to the sensation of pain. Strictly defined pain is the "subjective sensation or emotional experience" resulting from nociception and is an experience that is created in the cortex. Although invertebrates do not possess a central nervous system with a welldescribed cortex or similar structure it has been shown that a nociceptive response is present in invertebrates, that nociceptor cells are present (Nichols and Baylor, 1968) and that opioid systems have a functional role in invertebrate nociception (Kavaliers, Hirst, and Teskey, 1983; Fiorito, 1986; Kavaliers, 1988; Smith, 1991). However, no definitive answer exists for the debate of whether invertebrates perceive pain and would suffer emotional stress from it. The animals' response to mechanical, chemical, and electrical stimulus is seen by withdrawal and escape behaviors. This response is decreased or slowed when an analgesic is used (Kavalier and Hirst, 1983b). It is not yet clear if this decreased response results from a sedative effect of the drug or an analgesic effect. Until the question of pain in invertebrates is clearly answered, an analgesic should be given to any animal that is subjected to a painful procedure. On the other hand, the use of analgesics in invertebrate species is not common, and little research has been done examining methods of administration of analgesics, dosing, and the effects and impact of the different analgesics on the patient, the anesthesia, and the recovery.

Until more research is published, drugs with analgesic properties should be used to anesthetize invertebrates when invasive procedures are performed. Hypothermia and CO_2 do not possess analgesic properties and an inhalant agent is preferred. Although inhalant agents do not possess true analgesic properties, they do render mammalian patient insensible to painful stimuli when administered at sufficient anesthetizing doses. Unfortunately, the insensibility to painful stimuli only lasts as long as the animal is anesthetized, so if the procedure is expected to be associated with significant post operative pain, the administration of an analgesic is advisable. The use of diluted lidocaine (0.5 to 1 mg/ml) may be used for topical administration on the surgery site (do not exceed 5 mg/kg).

EUTHANASIA

Invertebrates play an important role in laboratory research. Despite improving regulations for euthanasia

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Table 13.1.

Invertebrate	Anesthetic Agent	Dosage	Induction Time	Recovery	Comments	Source
Gastropods Snails	Ethanol (5%) Ethanol (21.9%) +					Flores et al., 1982
Sea snails Abalone	menthol (0.042%) Sodium pentobarbital Isoflurane Magnesium sulfate or Mg Cl ₂ 2-Phenoxyethanol	$0.4 \mathrm{mg/ml}\mathrm{H}_2\mathrm{O}$ MAC: 1.09% Intracoelomic 0.5 -3 ml/L	8 hr <10 min 2-5 min 1-3 min	<10 min 5-20 min	10% Listerine® solution. Low mortality rate. Induction excitement. Good muscle relaxation.	Woodall et al., 2003 Martins-Sousa et al., 2001 Girdlestone et al., 1989 Clark et al., 1996 White et al., 1996
	Delizocalnie Magnesium sulfate Sodium pentobarbital	2-24 g/100 ml water 1 ml/L	5-8 min 15 min	3–35 min	$Larger\ size = Higher\ dosage.$	Edwards et al., 2000 White et al., 1996 Aquilina and Roberts, 2000
Cephalopods Cuttlefish	Ethanol	$15-30 \mathrm{ml/L} > 10.15 \mathrm{ml/L}$	1 min	20 min	Transient excitement.	Harms et al., 2006
Octopus	Mg Cl ₂ Ethanol	6.8 g/L 20 ml/L (2%)	6–12 min 4 min	2.5 min	Excitement, not effective	Gore et al., 2005 Andrews and Tansey, 1981
D. second	$Mg Cl_2 (7.5\%)/H_2 O$	50/50	1.5-13 min	1-10 min	In cold water species. Smooth induction and recovery.	Messenger et al., 1985; Culloty and Mulcahy, 1992
Divatives Oysters	Propylene phenoxetol (1% solution)	1-3 ml/L	6–15 min	<30 min		Norton et al., 1996; Mills et al., 1997
	Mg Cl ₂ (3.50%)		1-2 hr	90 min	Variable effects, long induction and recovery	Norton et al., 1996; Mills et al., 1997
Scallops	Mg Cl ₂ Chloral hydrate	30-50 g/L 4 g/L	2–6 min 10–25 min	10 min 20-30 min	Drug of choice. Variable effects, temperature dependent.	Heasman et al., 1995 Heasman et al., 1995
Arachnida Spiders and scorpions	Isoflurane/sevoflurane	3-5%/4-6%	5–15 min	3–20 min	Induction chamber system.	Pizzi, 2006; Melidone and Mayer, 2005; Cooper, 2001
Crustaceans Crayfish	Lidocaine Ketamine	0.4–1 mg/g IM 40–90 µg/g IM	1.5 min 1 min	5–30 min 1–2 hr, Dose	Variable response	Brown et al., 1996 Brown et al., 1996
Giant crab	Ketamine Xylazine	25–100 µg/kg IV 16–22 mg/kg IV	15-45 sec 3-5 min	8–40 min 25–45 min	Brief induction excitement. Bradycardia high dosages	Gardner, 1997 Gardner, 1997; Oswald, 1977
Crabs	Procaine	25 mg/kg IV	20-30 sec	2-3 hr	Excitatory phase, very	Oswald, 1977
Small crabs	Clove oil	$0.125 \mathrm{ml/L}$	16 min	2.5 hr	Euthanasia at long durations.	Gardner, 1997
Echinoderms Sea star	MgCl ₂ MS222 Menthol	7.5–8% 1–10g/L 2.5–5%				Harms, 2006; McCurley and Kier, 1995 Hendler et al., 1995; O'Neill, 1994 Costello and Henly, 1971

in different vertebrate species, no thorough guidelines or rules are available for euthanatizing invertebrates (AVMA, 2000), primarily because invertebrates are not covered by the US laboratory animal guidelines. Some countries take a more progressive position on the topic of animal welfare, and over the last few years suggestions for euthanasia of invertebrates have been made throughout the literature (Reilly, 2001; Cooper, 2006). Most commonly used methods are terminal anesthesia followed by physical destruction of the nervous system to assure death. There is an enormous need for improvement and research to assure ethically acceptable ways to euthanize members of this diverse group of species. As mentioned, the ability of invertebrates to respond to noxious stimuli and show different types of stress responses is well recognized.

It should be our goal as veterinarians to treat every living creature with respect and promote the well-being of these animals while decreasing the amount of stress put on them in every situation, even when the perception of pain is not fully understood. Euthanasia should be performed by a method that is effective, painless, and fast (Table 13.1). Owing to the fact that death is often difficult to verify in invertebrates, a physical destruction of the nervous system/primary ganglia is commonly added to a chemical method. It is important to keep in mind that the nervous system is different in every species and that decapitation alone may be an unsuitable technique. If death from an anesthetic overdose cannot be confirmed, or doubts in verification are present, physical methods (destruction, decapitation) are encouraged.

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14 Boney Fish (Lungfish, Sturgeon, and Teleosts)

Donald L. Neiffer

DO FISH NEED TO BE ANESTHETIZED?

Do fish feel pain? This question is the topic of ongoing debate with the answer having scientific as well as socioeconomic ramifications. Interested parties include researchers, commercial and sport fishermen, fish hobbyists, the pet industry, aquaculturists, public aquaria, veterinarians, fisheries biologists, and animal rights advocates. Although opinions are varied, stance on the subject is becoming increasingly polarized, a fact discernible upon review of the literature (Rose, 2002; Sneddon, Braithwaite, and Gentle, 2003; Sneddon, 2003; Chandroo, Duncan, and Moccia, 2004; Huntingford et al., 2006). Although many of the literary arguments are extensive, well organized, and persuasive, they appear biased and suggest a particular agenda. As each publication tends to build upon, refute, or at least cite earlier works, chronological evaluation of the literature is recommended.

Despite opposing views, proponents from both the "no-pain" and "pro-pain" camps set the same necessary requirements for pain perception: (1) appropriate neuroanatomy and neurophysiology; and (2) conscious awareness, whereby pain is a psychological experience associated with a "feeling" rather than just a sensory experience and behavioral reaction to injurious stimuli. Opinions on where the criteria appear phylogenetically and whether or not parallel systems have evolved serve as the foundation for the debate (Rose, 2002; Sneddon, 2003; Sneddon, Braithwaite, and Gentle, 2003; Chandroo, Duncan, and Moccia, 2004).

According to "no-pain" proponents, the two criteria for pain perception can only be satisfied by the existence of an advanced neocortex (Rose, 2002). Based on a large amount of empirical, neuroanatomical, physiological, and behavioral evidence, this group argues that fish, lacking a neocortex as well as homologous or homoplastic structures, are without conscious awareness and therefore are incapable of feeling pain. Any behavioral responses to noxious stimuli, being subcortical in

nature, are solely reflexive and occur without the awareness of pain. Any learned behavior (e.g., avoidance of electric shock) is associative or implicit, which occurs across species, even humans, without conscious awareness and so is no proof of pain perception (Rose, 2002).

Proponents of the "pro-pain" side of the equation submit a number of studies as evidence that fish do perceive pain. Although neuroanatomical and physiological evidence is presented, more emphasis is placed on behavioral studies as compared to the "no-pain" group. The underlying assumption is that fish, having a complex nervous system, exhibit some types of behavior that are indicative of their ability to form and act upon structured, internal neural representations of their internal and external environment (i.e., conscious awareness). Where learning is concerned, this group presents data they believe show that learning in fish is not limited to associative, but can involve greater cognitive ability, which infers conscious awareness. Working on the assumption that conscious awareness exists through behavioral evidence, the group presents evidence of the homological or homoplastic neuroanatomical and physiological structures similar to the neocortex of higher mammals, thus fulfilling the criteria of pain perception (Sneddon, 2003; Sneddon, Braithwaite, and Gentle, 2003; Chandroo, Duncan, and Moccia, 2004). As behavioral evaluation is potentially more subjective than neuroanatomical or physiological description, this approach has resulted in accusations by the "no-pain" group of anthropocentrism and incorrect extension of the human condition to all species (Rose, 2002). In response, the "pro-pain" advocates point out the inability to absolutely discount the presence of homologous or homoplastic structures and processes in species lacking an advanced neocortex (Sneddon, 2003; Sneddon, Braithwaite, and Gentle, 2003; Chandroo, Duncan, and Moccia, 2004).

One item both camps agrees on is that teleost fish are capable of nociception or the detection of noxious, tissue damaging stimuli that are sometimes accompanied by a reflex response (Rose, 2002; Sneddon, 2003; Sneddon, Braithwaite, and Gentle, 2003; Chandroo, Duncan, and Moccia, 2004). This mutual acceptance is based largely on experiments performed in a single species, rainbow trout (Oncorhynchus mykiss). In rainbow trout polymodal nociceptors have been characterized on the face, which have similar properties to those found in amphibians, birds, and mammals, including humans. Following exposure to stimuli known to be painful in humans, the behavior of rainbow trout is adversely affected as a result of stimulation of an intact nociceptive system. The "pro-pain" group believes higher processing is involved in the observed behavioral output which is similar to some of the responses of higher vertebrates and so is evidence of pain perception in fish (Sneddon, Braithwaite, and Gentle, 2003). The "no-pain" group, referring to the belief in the need of a neocortex, cites examples of similar responses in even higher vertebrates whereby conscious awareness is presumably prevented by injury to or removal of the cerebral hemispheres (Rose, 2002).

Although elasmobranchs are covered elsewhere, the available information regarding the apparent lack of nociceptive neuroanatomy in elasmobranchs (Rose, 2002; Sneddon, Braithwaite, and Gentle, 2003) and existence of nociceptive tissue in more primitive agnathans (lampreys and hagfishes) (Sneddon, Braithwaite, and Gentle, 2003; Chandroo, Duncan, and Moccia, 2004) should be reviewed by anyone interested in the evolution of nociception and controversy over pain perception in fish.

Several studies have demonstrated that fish treated with analgesics (i.e., morphine and butorphanol) were less affected behaviorally by noxious stimulants (Sneddon, 2003; Harms et al., 2005). In addition, morphine-treated goldfish (Carassius auratus) given naloxone responded more to noxious stimuli than those that did not receive it (Rose, 2002). Some "pro-pain" proponents use these results as evidence fish behavioral responses to noxious stimuli are not just simple reflexes, but instead are complex and require higher processing (Sneddon, 2003; Sneddon, Braithwaite, and Gentle, 2003; Chandroo, Duncan, and Moccia, 2004). "No-pain" proponents state that because opioids (e.g., morphine) produce anti-nociception at subcortical brainstem and spinal cord sites, claims of pain perception are not valid (Rose, 2002).

Fish display robust neuroendocrine and physiological stress responses to noxious stimuli. Acute and chronic stress negatively affect fish health. Consequently, there is a need to identify and then reduce these stressors in individuals and groups. Many drugs anesthetic or analgesic in humans and higher vertebrates reduce stress in fish. Whether or not they indicate fish feel pain is unnecessary for discussion of their use in fish management and medicine.

This author is an avid angler, has previous experience in fisheries science and the tropical fish hobby, and works as a veterinarian with public aquaria and, to a lesser extent, food fish production. As such, he can use any outcome of the controversy. How convenient. Although the author does not wish to push either agenda, he will err on the side of fish feeling pain or discomfort when addressing the appropriateness of chemical agents for specific uses in boney fish.

WHY CHEMICAL IMMOBILIZATION?

Chemical immobilization is routinely used to reduce excitement and hyperactivity related trauma that can occur during routine handling for vaccination, hormonal implants or injections, roe or milt collection, sorting, tagging, and transport of fish (Harms, 1999; Kumlu and Yanar, 1999; Ross and Ross, 2001; Myszkowski, Kamiński, and Wolnicki, 2003; Cooke et al., 2004). In addition to acute trauma causing mortality and morbidity, integument damage results in acute to chronic osmoregulatory disturbances and increased susceptibility to pathogens (Kumlu and Yanar, 1999; Ross and Ross, 2001). Chemical immobilization during transport reduces metabolism leading to decreased oxygen demand and waste (i.e., CO₂ and ammonia) production (Ross, 1984; Guo, Teo, and Chen, 1995; Cooke et al., 2004; Hoskonen and Pirhonen, 2004; Crosby et al., 2006).

Although examination and sample collection can be performed using manual restraint, for many minor procedures chemical immobilization is safer for both fish and handler. In addition, many procedures are preferably performed out of water. In most fish this stimulates struggling that requires restraint (Harms, 1995).

Major or surgical procedures require anesthesia to prevent movement and remove doubt in the debate over pain (Harms et al., 1995; Ross and Ross, 2001; Myszkowski, Kamiński, and Wolnicki, 2003). At the very least, movement and physiological changes in response to nociception are minimized.

EUTHANASIA

When necessary, overdosage of immobilization drugs is an acceptable means of euthanasia (Harms, 1995). Inhalant drugs at 5 to 10 times the anesthetic concentration for a particular species are usually chosen, although injectable agents can also be used (Ross, 1984). At the author's facility, MS-222 is most often used. However, many fish in large exhibits require induction first with parenteral drugs (e.g., medetomidine/ketamine), then euthanasia in an MS-222 bath. Alternatively, in fish too large for a bath, inhalant is poured directly over the gills (Harms, 1995). Except in some ram-ventilating species (e.g., tuna, family Scombridae, tribe Thunnini) cessation of opercular movement usually (but not always)

indicates a fish has expired. Cardiac asystole usually lags behind brain death since fish myocardial cells use local glycogen stores for energy and do not need blood glucose (Stetter, 2001). Use of Doppler flow probes, ultrasonography, or electrocardiography is recommended to confirm asystole. To be certain, additional anaesthetic drug or pentobarbitone are administered intravenously (IV) into the heart or caudal vein (Ross and Ross, 2001). Alternatively, cranial concussion, spinal transaction, or exsanguination are performed once the fish is deeply anesthetized (Harms, 1995).

STRESS AND ANESTHESIA

Fish restraint activates the hypothalamus-pituitary-interrenal (HPI) axis, resulting in cortisol release causing various secondary stress responses (Ross, 1984; Myszkowski, Kaiński, and Wolnicki, 2003; Small, 2003, 2005; Bressler and Ron, 2004). Cortisol release suppresses feeding and immune function, and alters reproductive productivity (Iversen et al., 2003; Myszkowski, Kamiński, and Wolnicki, 2003; Small, 2003, 2005; Bressler and Ron, 2004).

Although anesthesia minimizes handling stress, it is inherently stressful (Bressler and Ron, 2004) and a strong potentiator of catecholamine release, especially in salmonids (Rothwell et al., 2005). Anesthesiaassociated catecholamine release is likely caused by hypoxemia rather than acidemia or direct drug effects (Ross, 1984; Rothwell et al., 2005). However, unbuffered inhalants (e.g., MS-222) do induce a stress response. Hypoxemia is usually caused by drug-induced hypoventilation (decreased buccal movement). In air-breathing fish, hypoxemia can be exacerbated by preventing anesthetized fish access to the water's surface (Rantin et al., 1993, 1998). Hypoventilation with decreased water flow in the buccal cavity usually leads to reflex bradycardia and dorsal aortic hypotension, producing a progressive hypoxemia (Ross and Ross, 2001).

Despite the mentioned effects, chemical sedation or anesthesia produces a lower stress response when compared with drug-free handling and transport. This conclusion is based on comparison of circulating cortisol levels, as well as secondary indicators such as blood glucose, hematocrit (HCT), hemoglobin (Hgb), lactate, and osmolarity (Hseu et al., 1996; Bressler and Ron, 2004; Small, 2005; Crosby et al., 2006).

Of the commonly used drugs, only metomidate consistently and significantly blocks HPI activation (Iversen et al., 2003; Davis and Griffin, 2004) in a broad range of species; for example, red drum, *Sciaenops ocellatus* (Thomas and Robertson, 1991); Atlantic salmon, *Salmo salar* (Olsen, Einarsdottir, and Nilssen, 1995; Iversen et al., 2003); hybrid striped bass, *Morone chrysops x Morone saxatilis* (Davis and Griffin, 2004); and channel catfish, *Ictalurus* punctatus (Small, 2003).

The effect of clove oil (eugenol and isoeugenol) on cortisol secretion in fish is inconclusive. In channel catfish no significant increase in cortisol concentrations were observed following 30 minutes of undisturbed clove oil anesthesia or when subjected to confinement and reduced oxygen levels while exposed to isoeugenol (Aqui-STM)(Small, 2003, 2004, 2005). However, in the same species anesthetized with Aqui-STM and exposed to high unionized ammonia concentrations, cortisol was not suppressed (Small, 2004): in Atlantic salmon smolts, clove oil and Aqui-STM suppressed cortisol secretion while in adults only high dosages had the same effect (Iversen et al., 2003). In seabream (Sparus sp.) exposed to clove oil (Bressler and Ron, 2004) and rainbow trout (Small, 2005) exposed to both compounds, cortisol concentrations increased in response to handling. In gilthead seabream (Sparus aurata) exposed to clove oil (Bressler and Ron, 2004) and hybrid striped bass exposed to both compounds (Davis and Griffin, 2004), similar increases in circulating cortisol and glucose occurred. In red pacu (Piaractus brachypomus) exposure to eugenol increased glucose, HCT, and Hgb (Sladky et al., 2001), whereas in a related tropical freshwater species, tambaqui (Colossoma macropomum), no increase in glucose was noted (Roubach et al., 2005).

Except for low MS-222 dosages that depress (not block) the stress response in some fish (e.g., Chinook salmon, Oncorhynchus tshawytscha, and hybrid striped bass), inhalant anesthetic drugs minimally inhibit the HPI response (Davis and Griffin, 2004). Elevated cortisol and/or hyperglycemia occur in MS-222 exposed channel catfish (Small, 2003, 2005), Atlantic salmon (Olsen, Einarsdottir, and Nilssen, 1995), hybrid striped bass (Davis and Griffin, 2004), and red drum (Thomas and Robertson, 1991). Similar elevations occur in gilthead bream exposed to benzocaine (Bressler and Ron, 2004). Increased cortisol, with or without hyperglycemia, has also been associated with quinaldine exposure in red drum (Thomas and Robertson, 1991), channel catfish (Small, 2003), and hybrid striped bass (Davis and Griffin, 2004). In four marine teleost species, the physiological effects of 2-phenoxyethanol varied between species with significant elevations of HCT in red snapper (Lutijanus argentimaculatus), Hgb in grey mullet (Mugil cephalus), and osmolarity of black porgy (Acanthopagrus schlegeli), but no changes in milkfish (Chanos chanos) (Hseu et al., 1996).

Limited information on the effects of injectable drugs on the HPI response exists. In bonito (*Sarda chiliensis*) ketamine/medetomidine did not significantly alter HCT, Hgb, or glucose, although baseline values were not provided (Williams, Rollins, and Block, 2004).

It has been argued that the stress-induced corticosteroid response is not harmful and is essential for recovery from severe acute or prolonged stressors. A transient, relatively small elevation of cortisol does not necessarily reduce immunocompetency, but may instead bolster it (Thomas and Robertson, 1991; Small, 2003; Bressler and Ron, 2004; Davis and Griffin, 2004). Based on this argument, drugs that suppress the HPI (e.g., metomidate) are contraindicated in fish. However, the contrary argument is that typical husbandry and handling procedures do not result in high stress levels associated with chronic immunosuppression (Thomas and Robertson, 1991; Small, 2003; Bressler and Ron, 2004; Davis and Griffin, 2004). For anesthetics that do not block the HPI, the intensity and duration of the stress response either depends on the duration of exposure or is drug, dosage, and species dependent (Thomas and Robertson, 1991; Gomes et al., 2001; Bressler and Ron, 2004).

In addition to affecting the stress response, some anesthetics are immunosuppressive. This effect may be caused by direct interaction with immune components or indirectly through the nervous system. For example, in gilthead seabream, both humoral and cellular immune responses are significantly depressed by benzocaine (Bressler and Ron, 2004). However, clove oil does not cause significant immunosuppression in the same species, demonstrating the variability between species and drug effects (Bressler and Ron, 2004). Metomidate-associated blockade of the HPI is thought to prevent immunosuppression (Davis and Griffin, 2004).

TAXONOMY, ANATOMY, PHYSIOLOGY AND BEHAVIOR

Fish number upward of 30,000 species and comprise more than 40% of all extant chordates. Of these, teleosts (Teleostei of the class Acinopterygii) comprise about 96% of living fish species. Other groups include other members of class Acinopteryii or ray-fined fishes (sturgeon, gar, birchir, paddlefish, and bowfin), class Sarcopterygii or lobe-finned fishes (lungfishs and coelacanths), class Agnatha or jawless fish (hagfishes and lampreys), and class Chondrichthyes (elasmobranchs and chimeras) (Bond, 1996; Harms, 2003).

The majority of immobilization studies involve only a handful of teleosts. Extrapolation to all species is potentially harmful and negligent without consideration of the wide range of anatomic, physiological, and behavioral differences. For example, benzocaine kills cod (*Gadus morhua*) at the same dosage that is safe and effective in Atlantic salmon (Mattson and Riple, 1989; Hansen, Nymoen, and Horsberg, 2003). Even within families there can be marked variation in preferred environmental parameters. This affects the dosage selected and approach to using the same drug. Consequently, knowledge of taxonomy and natural history is essential for developing anesthetic regimens in fish.

Respiration

All fish have gills, although the degree of reliance on these structures for respiration varies across class, order, and family. Most fish force water over the gills through rhythmic movements of their lower jaw and opercula. However, some species use ram ventilation with minimal opercular movement and some (e.g., tuna, family Scombridae, tribe Thunnini) are obligate ram ventilators, with gilling alone not providing sufficient ventilation to meet metabolic demands. These species swim forward continuously with mouth slightly agape to develop the pressure head necessary for sufficient water flow over the gills. Failure to perfuse the gills during anesthesia results in suffocation (Bushnell and Jones, 1994; Brill and Bushnell, 2001). Tuna also rely on constant forward speed to produce lift from their pectoral fins for hydrostatic equilibrium (Brill and Bushnell, 2001). Consequently, during recovery of ram ventilating species, it is necessary to walk or hold the fish in sufficient flow until adequate voluntary forward motion of the sedated animal returns.

Many species (49 families within 17 orders) in response to hypoxic environments or other selective pressures have evolved anatomical, physiological, and behavioral adaptations to meet their ventilatory needs (Graham, 1997). In addition to elaboration of the basic gill design for improved oxygen extraction, a diverse array of accessory respiratory organs has evolved, with a number of species capable of using atmospheric air. For many, increased aerial gas exchange surface exists in portions of the alimentary canal (i.e., buccal and pharyngeal cavities), either as a direct proliferation of the respiratory surface in the lumen or as a single or a pair of pouches extending from it (Ishimatsu and Itazawa, 1993). Alternatively, branchial diverticula may develop, as in anabantoids (gouramis, bettas, climbing gouramis) (Graham, 1997).

Many species take in atmospheric air with a behavior termed aquatic surface respiration (ASR). The fish position their mouths to skim the air/water interface that is richer in oxygen. Some species (e.g., pacu, *Piaractus mesopotamicus*) respond to hypoxic conditions by developing temporary dermal swellings of the lower jaw to facilitate ASR (Rantin et al., 1993, 1998). Others (e.g., channids or snakeheads, anabantoids) employ alternate filling of an air-breathing chamber (laryrinth organ in anabantoids) with air and water during aerial ventilation (Ishimatsu and Itazawa, 1993).

Lungfish (the sister group to tetrapods) and polypterids (birchirs and reedfish) possess true lungs with ventrally situated pneumatic duct openings in the alimentary canal and not gas or "swim" bladders with their duct openings positioned laterally or dorsally (Graham, 1997). Of these, the African (*Propterus* sp.) and South American (*Lepidosiren* sp.) lungfish are obligatory airbreathers (Graham, 1997; Bassi et al., 2005). Although anatomically challenging, it is theoretically possible to cannulate the pneumatic duct of lungfish for administration of inhalant anesthesia. Alternatively, sterile percutaneous trocharization of the lung could be attempted.

Understanding the range of fish respiration is important for anesthesia for two reasons. First, inhalant uptake and induction rate are linked to oxygen demand. For fish that depend primarily or entirely on dissolved oxygen in water, induction rates are shorter compared with those of air-breathing species. Responding to confinement or hypoxic anesthetic baths, the latter pull air from the water surface and reduce opercular movement. Some may temporarily stop opercular activity (Hseu et al., 1997). Decreased brachial contact with the water results in a slower rate of anesthetic uptake. For example, 2-Phenoxyethanol induction in hypoxia tolerant tilapia (Oreochromis mosambicus) and molly (Poecilia velifera) is significantly longer than in black porgy (Acanthopagrus schlegeli) and Japanese sea perch (Lateolabrax japonicus) (Hseu et al., 1997). To circumvent this issue, injectable anesthetics can be used for induction of species capable of aerial respiration (e.g., anabantoids) (Bruecker and Graham, 1993). Second, although many fish that use an accessory respiratory organ retain gills for aquatic gas exchange, effective gill tissue is so reduced in some species (e.g., channids, lepidosirenid lungfish, and clariids or walking catfish) that they succumb or "drown" if denied access to atmospheric air (Ishimatsu and Itazawa, 1993; Peters et al., 2001). These species are maintained in very shallow water, or on a moist substrate, until capable of reaching the water-air interface regardless of anesthetic route used.

Although notable exceptions exist (e.g., tarpon, *Megalops atlanticus*), few marine species have evolved adaptations for hypoxic environments other than surface pipping or migrating from the area. Consequently, marine species may be less tolerant of hypoxic conditions during anesthesia in comparison with the freshwater species discussed in the preceding (Rothwell et al., 2005).

Metabolism

Most fish are ectothermic with metabolism dependent on ambient temperature. Although exceptions exist for some cold-adapted species, lower temperatures are usually associated with prolonged induction and recovery times during either inhalant or parenteral anesthesia (Gelwicks and Zafft, 1998). This effect is reversed at higher temperatures (Stehly and Gingerich, 1999; Gomes et al., 2001; Peters et al., 2001; Detar and Mattingly, 2004). During inhalant anesthesia this relationship is primarily related to altered respiratory rate. Blood acid-base status is temperature dependent. Increased temperature leads to academia and hypercapnia, which stimulate hyperventilation. This decreases induction and recovery times for drugs taken up or eliminated from the gills (Stehly and Gingerich, 1999; Aguiar, Kalinin, and Rantin, 2002).

Some fish have evolved various degrees of endothermy. They have the capacity to conserve metabolic heat in slow-twitch muscle, viscera, brain, and eyes, and

to elevate body tissue temperature above ambient (Bushnell and Jones, 1994). The most studied are tuna (family Scombridae), which have many anatomical and physiological adaptations that promote endothermy. Tuna gills have large surface areas and thin epithelia compared with other fish (Bushnell and Jones, 1994; Brill and Bushnell, 2001). For example, gill surface areas are approximately 7 to 9 times larger, and gill bloodwater barrier thicknesses an order of magnitude less than those of rainbow trout (Brill and Bushnell, 2001). The net result is enhanced oxygen uptake. Red cells with elevated hemoglobin are circulated by proportionally large hearts with high cardiac outputs (Bushnell and Jones, 1994; Blank et al., 2004) to well-vascularized tissues. High myoglobin levels and aerobic enzymes enhance tissue oxygen extraction. Enzyme activity is particularly high in muscle; aerobic oxidation rates are 3 to 5 times greater than other teleosts (Bushnell and Jones, 1994). Elevated enzymatic activity and countercurrent heat exchangers raise muscle temperatures (Cooper et al., 1994). Endothermy leads to increased rate of anesthetic uptake and metabolism compared to similarly sized ectothermic species. More primitive Scombrids (e.g., bonitos, seerfishes, and mackerels) are not endothermic and lack physiological characteristics of tuna such as the vascular countercurrent heat exchange mechanism. However, aerobic enzyme activity is similar and these scombrids represent a transition between ectothermy and tuna endothermy (Brill and Bushnell, 2001; Williams, Rollins, and Block, 2004).

All teleost fish have an anatomic separation between aerobic, slow-oxidative muscles and anaerobic, fast-twitch, glycolytic muscles. In many species, a distinct pattern of highly oxygenated slow-oxidative muscle runs along the midline of the body. Given the increased capillarization, injection of anesthetic agents into this region may result in more rapid induction times compared with injections administered elsewhere (Williams, Rollins, and Block, 2004).

Integument

Although most fish possess scales, marked variation in distribution and structure exist. This has implications for administration of parenteral drugs by hand and remote injection. Species (e.g., tarpon) that have large, hard scales are difficult to dart or pole syringe, whereas even large cobia (*Rachycentron canadum*) are relatively easy to inject.

For many fish the skin is a respiratory organ, responsible in some species for up to 30% of oxygen uptake (Bruecker and Graham, 1993). Most marine species have well-vascularized skin capable of significant cutaneous gas exchange (Ishimatsu and Itazawa, 1993). Although scale-less species (e.g., catfish, Siluriformes) are better designed for cutaneous respiration, capacity often varies with age class. Younger fish, regardless of size, tend to have thinner skin and less-developed scalation favoring

greater oxygen uptake (Myszkowski, Kamiński, and Wolnicki, 2003). Fish species that produce larvae lacking gills require skin respiration the first 9 to 15 days until full differentiation of secondary gill lamellae occurs (Oikawa, Takeda, and Itazawa, 1994). Like other respiratory organs, skin is a route for inhalant drug uptake and presumably excretion (Ferreira, Schoonbee, and Smit, 1984). The efficiency of uptake is dependant on scalation and, similar to gill tissue, lipid content of the skin. For example, some scaleless types of common carp (Cyprinus carpio) with high skin lipid content are much more efficient at cutaneous anesthetic uptake than rainbow trout with their small, densely packed scales and comparatively lower lipid content (Ferreira, Schoonbee, and Smit, 1984). In some instances, skin may actually be more efficient than other respiratory organs. For example, in the electric eel (Electrophorus electricus), quinaldine uptake across the skin was higher than the gills (Walsh and Pease, 2002).

Size and Age

Minimum effective anesthetic concentration is directly correlated with increasing body mass (Oikawa, Takeda, and Itazawa, 1994). This relationship is also true for toxic concentration. For example, MS-222 LC₅₀ increases with growth in rainbow trout (*Oncorhynchus mykiss*), brown trout (*Salmo trutta*), lake trout (*Salvelinus namaycush*), largemouth bass (*Micropterus salmoides*), and channel catfish (Oikawa, Takeda, and Itazawa, 1994).

ENVIRONMENTAL AND OTHER FACTORS

Temperature

In addition to metabolism, dissolved oxygen (DO) concentrations are influenced by temperature. At higher temperatures, DO decreases exacerbating any anesthetic induced hypoxia. Warmer temperatures also promote solubilization of inhalant anesthetics, whereas cooler temperatures promote precipitation.

рH

The pH of inhalant anesthetic solutions influences efficacy, possibly by affecting the ratio of charged to uncharged molecules. In general, decreased efficacy is seen as the pH drops owing to increased ionization that interferes with absorption. Unfortunately, most inhalant anesthetics (e.g., MS-222 and quinaldine) in solutions are acidic, requiring buffering agents (e.g., sodium bicarbonate) to neutralize the pH. In addition to promoting inhalant anesthetic efficacy (Ferreira, Schoonbee, and Smit, 1984), buffers prevent metabolic acidemia, a condition precipitated by anestheticinduced hypoxemia and anaerobic metabolism. Saltwater, with its higher pH and greater natural buffering capacity compared with freshwater, may not require addition of buffering agents (Ross, 1984; Oikawa, Takeda, and Itazawa, 1994; Harms, 1995; Harms, 1999; Ross and

Ross, 2001). The greater efficacy and safety of inhalant anesthetics in sea water was demonstrated in mullet (*Mugil cephalus*) (Sylvester, 1975). For a given concentration of MS-222, decreased efficacy and increased toxicity was noted in freshwater acclimated compared with saltwater housed mullet. At the author's institution, it is common practice to err on the side of caution and buffer marine water with sodium bicarbonate, particularly when multiple fish will be anesthetized in the same container.

Nitrogenous Compounds

Build-up of nitrogenous compounds, particularly ammonia and nitrite, can damage or induce changes in gill morphology that affect uptake and clearance of inhalant anesthetics. In addition, compromised oxygen uptake affects metabolism, including that of parenteral and inhalant anesthetic agents, and can lead to acidemia.

Drug Concentration or Dosage

At a given temperature, higher concentration (inhalants) or drug dosage generally decreases induction and increases recovery times. However, recovery time from some inhalants is independent of concentration (Hseu et al., 1997, 1998).

Drug Exposure Time

Increased inhalant anesthetic exposure time usually results in increased recovery time. This effect is often associated with progressive hypoxemia and metabolic acidemia owing to prolonged hypoventilation. Some inhalant drugs (e.g., MS-222) continue to increase in brain and muscle despite blood equilibration. Thus, an initially satisfactory drug dosage can produce progressively deeper anaesthesia and respiratory arrest, even during recovery when the fish is in anesthetic free water (Ross and Ross, 2001).

IMMOBILIZATION METHODS AND TECHNIQUES

General Suggestions

Before anesthetizing an unfamiliar species, perform a review of the available literature. Despite limited fish anesthesia publications, a literature search using the scientific name along with words or phrases such as "physiology," "anatomy," "site fidelity," "fecundity," "population assessment," etc., will identify studies that required sedation or anesthesia. Table 14.1, although listing anesthetic regimens for representatives of many families, is far from exhaustive and was accomplished, in part, as suggested in the preceding. Care is taken when using dosages and regimens from the literature because many studies use young or small fish. For example, drug dosages used in salmon smolts may not be effective in ocean-ranging adults.

Class Osteichthyes Taxa	Drug	Dose	Route	Wt./Age	Temp (°C)	Comments	Ref.
Subclass Sarcopterygii (Coelacanths/lungfish)							
Order Lepidosireniformes Family Lepidosirenidae Lepidosiren paradoxa (South American Lungfish)	Benzocaine	Induction: 1 g/L Maintenance: 0.25 g/l	呂	$577 \pm 12\mathrm{g}$	25	Obligate air breathers; prevent drowning. Induction: within 10 min. Maintained by flushing 0.25 g/l solution over gills. Recovery within 1 hr.	Bassi, 2005
Family Protopteridae Protopterus annectens (West African Lungfish)	Medetomidine plus ketamine	0.053 mg/kg 5.26 mg/kg	M	1.33 kg		Obligate air breathers, prevent drowning. Provided mild sedation, but not adequate for diagnostics without physical restraint. No reversal given. Recommend higher dose.	Neiffer, unpub.
Subclass Actinopterygii Subdivision Chondrostei (sturgeons, paddlefish)							
Order Acipenseriformes Family Acipenseridae	;	,	ļ	;			
Acipenser oxyrhynchus desotoi (Gulf of Mexico Sturgeon)	Medetomidine plus ketamine	0.06 mg/kg 6 mg/kg	Z	4 -yr-old $3.6 \pm 1.2 \mathrm{kg}$	21.6 ± 3.1	Light plane of anesthesia for minor diagnostic procedures within 10 min. Mild bradycardia and resniratory depression noted.	Fleming, 2003
	Atipamezole	0.30 mg/kg	IM			Atipamezole administered 30 min after immobilizing agents. Full recovery by 30 min. No mortality.	
	Propofol	6.5 mg/kg	2	4 -yr-old $3.6 \pm 1.2 \text{ kg}$	21.6 ± 3.1	Light plane of anesthesia for minor diagnostic procedures within 5 min. Mild bradycardia and respiratory depression noted with latter persisting for 60 min. Fish remained quiet and unresponsive for 40 min. At 60 min 70% were struggling at pre-injection levels. All fish fully recovered within 190 min No mortality.	Fleming, 2003
Acipenser transmontanus (White Sturgeon)	Clove Oil	$50-100 \mathrm{mg/L}$	Z	206–363 g		Induction: 3–6 min. Exposed for 10 min. Recovery: 4.5–8.5 min. No mortality.	Taylor, 1999
Acipenser ruthenus × Huso huso (Hybrid Sterlet and Beluga Sturgeon)	Ketamine MS–222	77–88 mg/kg 100–125 mg/L	Z Z	5-7.7 kg 1.36-2.34 kg		Induction: $4-7$ minutes. Effect lasted 6 hrs. Variable effect from mild sedation to light anesthesia. $N = 10$.	Williams, 1988 Neiffer, unpub.

Table 14.1. (Continued)							
Class Osteichthyes Taxa	Drug	Dose	Route	Wt./Age	Temp (°C)	Comments	Ref.
Subdivision Teleostei							
Order Anguilliformes (Eels) Family Anguillidae							
Anquilla reinhardtii (Long-finned Eel)	Benzocaine dissolved in	7/8m 08-09	Z	Adults	17–25	Induction within 6 min.	Walsh, 2002
	Clove Oil	$100 \mathrm{mg/L}$	Z	Adults	17–25	Induction within 6 min.	Walsh, 2002
Anquilla rostrata (American Eel)	MS-222	75 mg/L	呂			Sedation rated excellent. Examination performed.	Neiffer, unpub.
Family Muraenidae Gymnothorax funebris (Green Moray)	MS-222	50-100 mg/L	Z	Adults		Suitable for examination. Animals that gulp air at surface may take longer to induce. Make sure animal is enclosed in a confined area since	Chittick, unpub.
<i>Gymnothorax vicinus</i> (Purplemouth Moray)	MS-222	50-100 mg/L	Z	Adults		prone to leaping. Suitable for examination. Animals that gulp air at surface may take longer to induce. Make sure animal is enclosed in a confined area since prone to leaping.	Chittick, unpub.
Order Batrachoidiformes							
Opsanus beta (Gulf Toadfish)	MS-222	670 mg/L buffered with NaOH	呂	Sexually mature fish	24-26	Once fish was induced they were wrapped in anesthetic solution soaked paper towels for 30-minute surgical placement of venous cannula. Species considered tolerant of air exposure, and it	Gilmour, 1998
Opsanus tau (Oyster Toadfish)	MS-222	50-250 mg/L	Z	Adults $675 \pm 46 \text{ g}$	20	was not necessary to Irrigate gills. pH = 8. Slight sedation at 50 mg/L. Decreasing respiratory rate and ability to maintain equilibrium from 100 to 250 mg/L. Cessation of voluntary respiratory activity at 300 mg/L. These latter fish resumed gilling 14 min after anesthetic withdrawal and all fish regained equilibrium within 23 min of anesthetic withdrawal.	Palmer, 2004
Order Beryciformes Family Holocentridae Holocentrus ascensionis	MS-222	70-85 mg/L	Z	160-500 g		Variable sedation (mild to heavy) for examination.	Neiffer, unpub.
(Long-Jawed Squirrelfish) Myripristis jacobus (Blackbar Soldierfish)	MS-222	50–100 mg/L	Z	140-390 g		Variable sedation (mild to heavy) for examination.	Neiffer, unpub.
Order Characiformes Family Characidae Brycon cephalus (Matrinxa)	MS-222 buffered with CaCO ₃	150 mg/L	Z	Juveniles 31.56 \pm 8.08 g	25	Time to anesthesia: 5.62 ± 0.53 min. Anesthesia duration: 10 min. Recovery: $5.19 + 3.07$ min. Mortality: 0% at 150 mg/L, 16.7% at 200 mg/L, and 33.3% at 300 mg/L. Pronounced stress response at 200 and 30 mg/L. pH = 6.3 .	Roubach, 2001

Piaractus brachypomus (Red Pacu)	MS-222 buffered 1:1 with	100, 200 mg/L	Z	4-yr-old adults 500–727 g	20-23	Induction: 100 mg/L average 550 s ; 200 mg/L average 350 s . Recovery: $300-500 \text{ s}$. pH = $5.5 = 7.0$	Sladky, 2001
	Eugenol dissolved in 95% ethanol (1:9)	50, 100, 200 mg/L	呂	4-yr-old adults 500-727 g	20-23	Induction: 50 mg/L average 300 s ; $100 \text{ \& } 200 \text{ mg/L}$ average 200 s . Recovery: $550-600 \text{ s}$. Resuscitation required in $>50\%$ fish exposed to $100-200 \text{ mg/L}$. $nH = 5.5-7.0$	Sladky, 2001
Piaractus mesopotamicus (Pacu Caranha)	Benzocaine (1g dissolved in 0.1 liter ethanol)	7/8m 66	Z	Adults 315.2-745.2 g	15-35	Used for surgical implantation of ECG electrodes, buccal, and opercular catheters. Sufficient level of anesthesia without interruption of spontaneous	Aquiar, 2002 Rantin, 1998
Colossoma macropomum (Tambagui)	Benzocaine dissolved in acetone (10 g/100 ml)	100–150 mg/L	Z	Juvenile $9.32 \pm 3.7 \mathrm{g}$	24	Induction: $0.11-1.01$ min. Recovery following exposure for 10 min: $2.32-9.04$ min. Recovery following exposure for 30 min: 30 ± 20 min. Fish exposed to ≥ 220 mg/L exhibited stress response.	Gomes, 2001
	Eugenol dissolved in alcohol to make 1:2 stock solution	65 mg/L	Z	Juveniles $56.6 \pm 7.7 \text{ g}$	26-27	Stage necessary for handling reached in 1.45 min and a surgical stage in 2.54 min. Recovery: 6.82 ± 3.73 min. Exposure for 30 min was not associated with mortality. Dose up to 100 mg/L	Roubach, 2005
		65 mg/L	<u>Z</u>	Sub-adults $1100 \pm 90.7 \mathrm{g}$		Stage necessary for handling in 1.48 min and surgical stage in 3.77 min. Exposure for 30 min. Recovery: 3.79 ± 0.89 min. No mortality. Dose up to 100 mg/L considered safe.	
Family Erythrinidae Hoplias lacerdae	Benzocaine	50 mg/L	Z	Adults	25 ± 1	Provided light anesthesia for brief procedures	Rantin, 1993
(Giant Irahira)	(1 gram in 0.1 liter ethanol)			3/5 ± 4/ g		including ECG electrode and buccal catheter placement. Shontaneous breathing present	
Hoplias malabaricus (Tiger Characin)	Benzocaine (1 gram in 0.1 liter ethanol)	50 mg/L	Z	Adults $312 \pm 47 g$	25 ± 1	Provided light anesthesia for brief procedures including ECG electrode and buccal catheter placement. Spontaneous breathing present.	Rantin, 1993
Order Cypriniformes Family Cyprinidae							
Carassius auratus (Goldfish)	2-PE	0.25-0.35 ml/L	Z	$3.93 \pm 1.99 \mathrm{g}$	24	Provided light sedation. Provided anesthesia with loss of equilibrium	Kaiser, 1998
Ctenopharyngodon idella (Grass Carp)	MS-222	100 mg/L for induction; 75 mg/L for	呂	1.0-2.5 kg	22	Induction within 5 min. Allowed for surgical implantation of radio transmitters. Recovery took 5–25 min. Mortality occurred with 100 mg/L at teamorathies. 31°C	Schramm, 1984
	2-PE mixed with 500 ml tank water and added to chamber.	0.2 ml/L	<u>Z</u>	Brood stock 3–12 kg	25	Induction to light sedation in 2–3 min. Females stripped of ova with this dose. Induction to anesthesia in 5–10 min. Males stripped of milt with this dose	McCarter, 1992

Table 14.1. (Continued)							
Class Osteichthyes Taxa	Drug	Dose	Route	Wt./Age	Temp (°C)	Comments	Ref.
Cyprinus carpio (Koi/Common Carp)	MS-222 MS-222 buffered with NaHCO ₃	100–200 mg/L 200 mg/L	<u> </u>	123 ± 53 g 144 ± 44 g	22–27 23–25	Utilized for exploratory celiotomy. $pH = 6.9-7.5$ Induction within 2 min. Level sufficient for deep IM injection and phlebotomy. Recovery within 2 min. $pH = 7.4-7.6$	Harms, 2005 Yanong, 2005
	Alphaxalone– alphadolone (Saffan)	0.3 ml/kg	IM	2 kg		Sedation with partial loss of equilibrium. Able to be netted, but responsive.	Harvey, 1987
Epalzeorhynchos bicolor (Red_Tail Black Shark)	(Sanan) MS-222	$100 \mathrm{mg/L}$	Z	Juveniles 1 4 + 0 4 α	25.5	An esthesia sufficient for handling and vaccination. $_{\text{oH}} = 7.5$	Russo, 2006
(New-Tall Black Shalk) Hypophthalmichthys molitrix (Silver Carn)	2-PE mixed with	0.2 ml/L	Z	Brood stock $\frac{2}{3}$ 12 $\frac{1}{2}$	25	$p_{11} = 7.3$ Induction to light sedation in 2–3 min.	McCarter, 1992
(SHVEL CALP)	water and added to chamber.	0.4 ml/L		3-12 ng		Induction to anesthesia in 5–10 min.	
Phoxinus erythrogaster (Southern Redbelly Dace)	MS-222 buffered with NaHCO ₃	60 mg/L	Z	Adults and Juveniles	11-21	Induction to total loss of equilibrium in 5-13 min. Recovery: <2 min with faster recovery at higher temperatures. Mortality: 0% off = $70-79$	Detar, 2004
	Clove Oil dissolved in ethanol (1:10)	40-60 mg/L	Z	Adults and Juveniles 0.35–4.46 g	11–21	Induction to total loss of equilibrium within 3 min. Recovery: <5 min with faster recovery at higher temperatures. No mortality. pH = 7.0–7.9	Detar, 2004
Phoxinus cumberlandensis (Rlackside Dace)	Clove Oil	$40\mathrm{mg/L}$	Z	Adults and	4-19	Used for anesthesia in the field during elastomer tag	Detar, 2004
Rhinichthys atratulus (Blacknose Dace)	MS-222 unbuffered with significant pH drop.	300-500 mg/L	Z	Adults		Light anesthesia within 3 min. Allowed for handling. Recovery following 9 min exposure: 4–7 min. Exposure to this dose range beyond 15 min associated with mortality.	MacAvoy, 1997
Rutilus rutilus (Roach)	Clove oil dissolved in 95% ethanol at 1:10 ratio.	4 mg/L	Z	71 g	15	provided sedation for 6 hrs without loss of equilibrium at which time fish removed from anesthetic. Considered useful for transport. No mortality	Hoskonen, 2004
<i>Tinca tinca</i> (Tench)	2-PE	0.5 g dm ⁻³	Z	Juveniles 0.08–1.82 g	25	Induction time: 2.2-12.6 min. Recovery after 15 min exposure: 1.1-3.3 min. Recommended for short term anesthesia. pH = 7.5-8.0	Myszkowski, 2003
Order Cyprinodontiformes Family Poeciliidae							
Poecilia velifera (Sailfin Molly)	2-PE	7/8m 009	Z	Adults 1.56 + 0.27 g	23	Induction: 7.50 \pm 11.97 min. Recovery (fish placed in fresh water immediately after induction): 1.28 \pm 2.53 min.	Hseu, 1997
Xiphophorus maculatus (Southern Platvfish)	MS-222	$30\mathrm{mg/L}$	Z	Adults 1.71 + 0.36 g		Provides light sedation.	Guo, 1995
	Metomidate	$1\mathrm{mg/L}$	Z	Adults 1 71 + 0 36 g		Provides light sedation.	Guo, 1995
	Quinaldine sulfate	$10\mathrm{mg/L}$	Z	Adults 1 71 + 0 36 g		Provides light sedation.	Guo, 1995
	2-PE	220 mg/L	呂	Adults $1.71 \pm 0.36 \mathrm{g}$		Provides light sedation.	Guo, 1995

Order Gadiformes Family Gadidae							
Gadus morhua (Atlantic Cod)	MS-222	75 mg/L	Z	$84 \pm 5 \mathrm{g}$	8.4	Anesthesia within 4 min. Exposure time 2.8–3.4 min. Recovery time 3.7–7.1 min.	Mattson, 1989
	Benzocaine dissolved in ethanol	$40\mathrm{mg/L}$	Z	$101 \pm 6 \mathrm{g}$	9.5	Anesthesia reached within 3 min. Exposure time 2.1–3.2 min. Recovery time 3.9–10.8 min. Mortality 50% at 75–100 mg/L.	Mattson, 1989
	Metomidate	5 mg/L	Z	101 ± 6 g	9.6	Anesthesia reached within 4 min. Exposure time 4.8–10.8 min. Recovery time 8.2–19.2 min. Used for sorting and handling broodstock.	Mattson, 1989
Order Gasterosteiformes Family Syngnathidae Hippocampus reidi	MS-222	25 mg/L	Z			Provided mild sedation.	Neiffer, unpub.
(Longshout seanorse) <i>Syngnathus scovelli</i> (Pipefish)	MS-222	75 mg/L	Z			Sedation rated as good. Topical treatments performed.	Neiffer, unpub.
Order Gonorynchiformes Family Chanidae Chanos chanos (Milk Fish)	2-PE	400 mg/L	Z	$23.99 \pm 1.07 \text{ g}$	28	Provided total loss of equilibrium allowing phlebotomy. Hseu, 1996	y. Hseu, 1996
Order Lophiiformes Family Antennariidae Antennarius ocellatus	MS-222	30-80 mg/L	Z	350-450 g		Sedation rated fair to excellent (higher doses better).	Neiffer, unpub.
(Ocellated Frogilsh) Antennarius striatus (Striated Froefish)	MS-222 buffered with NaHCO.	100 mg/L	Z	Adults		Examination and topical treatments performed. Diagnostics performed.	Yanong, 2003
Histrio histrio (Sargassumfish)	MS-222	$30\mathrm{mg/L}$	Z			Sedation adequate for examination and injections.	Neiffer, unpub.
Order Osteoglossiformes Family Mormyridae Gnathonemus petersii (Elephantnose fish)	Alphaxalone- alphadolone	2 mg/L for induction 1.5 mg/L for maintenance	呂	Average 15 g and 15 cm	23	Loss of equilibrium and cessation of opercular movement at 20 min. Recovery took average of 17 min following 2.5-hr exposure.	Peters, 2001
Order Perciformes Family Acanthuridae							
Acanthurus bahianus (Ocean Surgeonfish)	MS-222	50-75 mg/L	Z			Sedation rated fair to good. Examinations performed.	Neiffer, unpub.
Acanthurus chirurgus (Doctorfish)	MS-222	50-75 mg/L	Z			Provided surgical anesthesia for enucleation.	Neiffer, unpub.
Acanthurus coeruleus (Blue Tang)	MS-222	85 mg/L	Z			Sedation rated excellent. Examination and topical treatment performed	Neiffer, unpub.
Acanthurus leucosternon	MS-222	50-78 mg/L	Z			Sedation rated excellent. Diagnostic examination	Neiffer, unpub.
(rowder bure surgeomisn) Acanthurus sohal (Sohal Tang)	MS-222	$50\mathrm{mg/L}$	Z			performed. Sedation rated good. Diagnostic examination performed.	Neiffer, unpub.

Table 14.1. (Continued)							
Class Osteichthyes Taxa	Drug	Dose	Route	Wt./Age	Temp (°C)	Comments	Ref.
Family Carangidae Carangoides rubber (Bar Jack)	MS-222	75 mg/L	Z	70g		Sedation rated as good. Adequate for examination	Neiffer, unpub.
Caranx crysos (Blue Runner)	MS-222	$80\mathrm{mg/L}$	Z			Sedation rated as good. Diagnostic examinations	Neiffer, unpub.
	Alphaxalone- alphadolone	1.5 ml/kg	IM	1.5 kg		performed. Anesthesia with marked depression of ventilation	Harvey, 1987
Caranx latus (Horse-eye Jack)	(Saffan) MS-222	70-80 mg/L	Z			Sedation rated as good to excellent. Examinations	Neiffer, unpub.
Caranx melampygus (Ulua)	Metomidate	80-100 mg/kg	IM	20–35 kg		Sedation with partial loss of equilibrium within 2–5 min. More than one dart used to deliver total dose Able to be netted, but responsive. Recovered	Harvey, 1987
	Alphaxalone- alphadolone	0.4 ml/kg	IM	18 kg		within 30 mm. Light sedation with partial loss of equilibrium. Directed net avoidance.	Harvey, 1987
Selene vomer (Lookdown)	(Sarran) MS-222	75-125 mg/L	Z			Varied effect from mild sedation to light anesthesia	Neiffer, unpub.
<i>Seriola lalandi</i> (Yellowtail Amberjack)	Tiletamine- zolazepam (35 mg active powder in gel capsules)	8–9 mg/kg	Ю	6–9 kg		Sedation first noted at 6–8 hr. At this point fish trapped in hand-held net for examination, phlebotomy, and translocation. Animal remained responsive to the touch. Maximum sedation at approximately 12 hr. Recovery ranged from 12–48 hr. Mortality: 4/14 died owing to unplanned consumption of additional oral doses	Steers, 2001
Seriola dumerili (Greater Amberjack)	Metomidate	80 mg/kg	IM	9 kg		(total averaging 15–20 mg/kg). Sedation with partial loss of equilibrium within 2–5 min. Able to be netted, but responsive.	Harvey, 1987
	Alphaxalone- alphadolone	0.3 ml/kg	IIM	8 kg		Recovered within 30 min. Sedation with partial loss of equilibrium. Able to be netted, but responsive.	Harvey, 1987
Trachinotus carolinus (Florida Pompano)	(5411411) MS-222	75-100 mg/L	Z			Provided sedation to light anesthesia for examinations, tagging, and ocular surgery.	Neiffer, unpub.
Family Centrarchidae Lepomis macrochirus (Bluegill Sunfish)	Isoeugenol (AQUI-S)	20 mg/L	Z	s.	12 ± 2	Induction within 3 min. Total exposure time = 15 min. Recovery within 8 min. Useful for	Stehly, 1999
		20 mg/L	Z	213 ± 118 g Fry-fingerlings 0.54 ± 0.2 g		basic handling procedures, pH = 8.1 Induction within 4.1 min. Total exposure time ≤ 15 min. Recovery within 5 min. Useful for	
Micropterus salmoides (Largemouth Bass)	MS-222	50 mg/L for induction; 25 mg/L for maintenance				basic handling procedures. pH = 8.1 Provided sufficient sedation for transport.	Cooke, 2004

	Clove oil dissolved in ethanol (1:9)	5-9 mg/L		Finger-lings 21 and subadults	Time to deep sedation: 368 s. Sufficient for transport (reduced activity while maintaining equilibrium).	
		15-20 mg/L			recovery: 11.5. Time to moderate anesthesia 651 s. Recovery: 1,699 s.	
Family Centropomidae Centropomus undecimalis (Common Snook)	MS-222	50-60 mg/L	Z		Provided mild sedation for diagnostic examinations.	Neiffer, unpub.
Lates calcarifer (Asian Sea Bass)	Clove oil dissolved in boiled water	7/8m 6-9		$42 \pm 9.74 \mathrm{g}$ 29-30	Induction: 1.8–4.5 min. Exposed to clove oil for 4 min. Recovery: 0.5–5.0 min. No mortality though some distal gill filament necrosis noted with repeated exposure to 9 mg/L.	Afifi, 2001
Family Cichlidae Amphilophus citrinellus (Cichlasoma citrinellum) (Midas cichlid, Red Devil)	MS-222	150 mg/L for induction; 60 mg/L for	Z	800g	Induction in 8 min. Flow rate of maintenance solution = 3 I/min. Procedure duration (partial swim bladder resection) = 71 min	Lewbart, 1994
	Ketamine	mannenance. 30 mg/kg	2	$206 \pm 36 \mathrm{g}$ 22 ± 2	Fish sedated first in buffered MS-222 (100-125 mg/L) for 8–10 min at which point fish became unresponsive. Fish removed to from bath and ketamine was injected. Induction: <10 sec. In some fish complete cessation of ventilation occurred while in other intermittent coughing or rapid ventilation was noted. Anesthesia lasted 1–41 min	Bruecker, 1993
Oreochromis mossambicus (Mozambique Tilapia)	2-PE	600 mg/L	Z	Juveniles 30 $3.83 \pm 0.55 \mathrm{g}$	with balance regained at 57–263 min. Induction: 7.43 + 13.25 min. Recovery (fish placed in fresh water immediately after induction): 1.38 + 1.77 min.	Hseu, 1997
Family Chaetodontidae Chaetodon pelewensis	MS-222	50-75 mg/L	Z	$100\mathrm{g}$	Sedation rated as good. Examination performed.	Neiffer, unpub.
(refewensis butterny) Chaetodon semilarvatus (Dod 1:20d butterfich)	MS-222	75-80 mg/L	Z		Provided mild to heavy sedation. Examination and	Neiffer, unpub.
(red-mied butternynsn) Heniochus acuminatus	MS-222	7/8m 06	Z		topical treatments benotined. Sedation rated as good. Diagnostic examination	Neiffer, unpub.
(black and wonte nemocrius) Heniochus sp. (Bannerfish)	MS-222	90 mg/L	Z		performed. Provided heavy sedation for diagnostic examinations.	Neiffer, unpub.
Family Ephippidae Chaetodipterus faber (Atlantic Spadefish)	MS-222	50-100 mg/L	Z	0.22–2.32 kg	Effect varied from mild sedation at lower doses to surgical anesthesia at 100 mg/L . $n = 11$.	Neiffer, unpub.
Family Gobiidae Afurcagobius tamarensis (Tammar River Goby)	Clove oil in ethanol at	40 mg/L	Z	18	Induction within 3 min. Recovery within 5 min. Sufficient for handling and measurement.	Griffiths, 2000
Bathygobius cocosensis (Cocos frill–goby)	Clove oil in ethanol at ratio 1:5	40 mg/L	N	18	Induction within 3 min. Recovery within 5 min. Sufficient for handling and measurement.	Griffiths, 2000

Table 14.1. (Continued)							
Class Osteichthyes Taxa	Drug	Dose	Route	Wt./Age	Temp (°C)	Comments	Ref.
Favonigobius lateralis (Goby)	Clove oil in ethanol at ratio 1:5	40 mg/L	呂		18	Induction within 3 min. Recovery within 5 min. Sufficient for handling and measurement.	Griffiths, 2000
Family Grammatidae Pseudoanthias sp. (Anthias sp.)	MS-222	$77~\mathrm{mg/L}$	Z	Adult		Sedation rated excellent. Diagnostic examination	Neiffer, unpub.
Gramma loreto (Royal Gramma)	MS-222	65-90 mg/L	Z			Performed. Sedation rate as good. Diagnostic examinations performed.	Neiffer, unpub.
Family Haemulidae Haemulon chrysargyreum	MS-222	$100\mathrm{mg/L}$	Z			Provided surgical anesthesia for kidney culture.	Neiffer, unpub.
Haemulon flavolineatum	MS-222	$100~\mathrm{mg/L}$	Z			Provided surgical anesthesia for enucleation and	Neiffer, unpub.
(French Grunt) Haemulon plumieri (Mhito Gaust)	MS-222	85-100 mg/L	Z			kidney cuiture. Sedation rated good. Examinations performed.	Neiffer, unpub.
(winte Grunt) Haemulon sciurus (Bluestripe Grunt)	MS-222	30-90 mg/L	Z			Most sedations rated as good. Diagnostic examinations, injections, and enucleation	Neiffer, unpub.
Haemulon melanurum	MS-222	80 mg/L	Z			(1 case) performed. Sedation rated as good. Examination performed.	Neiffer, unpub.
(Cottonwick) Haemulon aurolineatum	MS-222	100 mg/L	Z			Sedation rated good. Examination performed.	Neiffer, unpub.
Anisotremus virginicus (Porkfish)	MS-222	$100 \mathrm{mg/L}$	Z			Provided surgical anesthesia for enucleation and kidney culture.	Neiffer, unpub.
Family Kyphosidae Girella elevate (Black Drummer)	Clove oil in ethanol at	40 mg/L	Z		18	Induction within 3 min. Recovery within 5 min. Sufficient for handling and measurement.	Griffiths, 2000
Microcanthus strigatus	ratio 1:5 MS-222	75 mg/L	Z			Provide heavy sedation.	Neiffer, unpub.
(Convict Tang) Scorpis lineolatus (Silver Sweep)	Clove oil in ethanol at ratio 1:5	40 mg/L	Z		18	Induction within 3 min. Recovery within 5 min. Sufficient for handling and measurement.	Griffiths, 2000
Family Labridae Halichoeres radiatus (Puddingwife) Thalassoma duperreyi	MS-222 MS-222	50-100 mg/L 90 mg/L	Z Z			Sedation rated as good. Diagnostic examinations performed. Sedation rated as good. Diagnostic examinations	Neiffer, unpub. Neiffer, unpub.
(Saddle Wrasse) Family Lateolabracidae <i>Lateolabrax japonicus</i> (Japanese Seaperch)	2-PE 2-PE	400 mg/L 400 mg/L	召召	48.98 ± 3.47 g Juveniles 4.4 + 0.86 g	29	performed. Provided total loss of equilibrium allowing phlebotomy. Hseu, 1996 Induction: 2.13 + 0.45 min. Recovery (fish placed Hseu, 1997) In fresh water immediately after induction):	y. Hseu, 1996 Hseu, 1997
						0.69 + 0.15 min.	

	2-PE	400 mg/L	Z	Juveniles $4.8 \pm 1.46 \mathrm{g}$	24	Induction: 1.75 \pm 0.16 min. Recovery (fish placed in non-medicated water immediately after induction): 0.49 \pm 0.08 min.	Hseu, 1997
Family Lobotidae Lobotes surinamensis (Tripletail)	MS-222	80-90 mg/L	Z			Sedation sufficient for examinations and jaw debridement (one individual).	Neiffer, unpub.
Family Lutjanidae Lutjanus apodus (Schoolmaster) Lutjanus sp. (Snapper)	MS-222 Metomidate	125 mg/L 50 mg/kg	ZZ	14 kg		Provided surgical anesthesia for kidney culture. Anesthesia with marked depression of ventilation.	Neiffer, unpub. Harvey, 1987
Ocyurus chrysurus (Vollowtail Spanner)	MS-222	75-85 mg/L	Z	$50-120\mathrm{g}$		The original rate of the second of the seco	Neiffer, unpub.
(Tenowian Shapper)	Medetomidine plus ketamine	1.1–1.7 mg/kg 27–42 mg/kg (ratio M:K averages 24:1)	IM	2.35-3.65 kg $(n=6)$		All fish injected by dives using jab stick. Initial effect seen in 4–12 min. For complete injections, mild to moderate sedation achieved. Fish netted and transferred to MS-222 bath for phlebotomy. Fish culled as part of disease surveillance and thus	Neiffer, unpub.
Lutjanus argentimaculatus (Mangrove Red Snapper)	2-PE	400 mg/L	Z	$39.21 \pm 2.08 \mathrm{g}$	59	no reversa agent given. Provided total loss of equilibrium allowing phlebotomy. Hseu, 1996	7. Hseu, 1996
Family Moronidae <i>Dicentrarchus labrax</i> (Sea Bass)	Quinaldine sulfate with diazepam	7.5 mg/L 2 mg/L	Z	Juveniles 8–9 g	24-25	Induction time 1–2 min. Recovery time 4–6 min. Provides deep anesthesia suitable for marking, surgery, and handling, *Note: quinaldine sulfate alone at 15 mg/L associated with 10% mortality and at 20–25 mg/L, associated with 30–100% mortality.	Yanar, 2001 y,
	Quinaldine sulfate with diazepam	5 mg/L 2 mg/L	Z	Juveniles 8–9 g	24–25	Induction time 1–2 min. Recovery time 3–5 min. Provides light anesthesia suitable for transportation. $nH = 7.9-8.2$	Yanar, 2001
Morone saxatilis (Striped Bass)	MS-222	20 mg/L	Z	Adult, 48–81 cm 2	21	Prior to placement in bath, gills were sprayed twice with MS-222 solution (3,200 mg/L). Procedure: Mock intra-coelomic transmitter placement. Induction: 38–58 s. Recovery after 5 min exposure to drug: 156–272 s. No mortalities. *Note from author (DN)-species appears to be sensitive to MS-272.	Jennings, 1998
	Benzocaine dissolved in 100% ethanol	55-80 mg/L	Z	Juvenile and Adults 0.118-3.5 kg	11-22	Induction in 3 min. Recovery in 1.5–14.25 min.	Gilderhus, 1991
Morone saxatilis × chrysops (Hybrid Striped Bass)	MS-222 Clove oil Isoeugenol (Aqui-S) Quinaldine Sulfate Metomidate	25 mg/L 8 µl/l 3.6 mg/L 8.3 mg/L 1.5 mg/L		87 ± 24.4 g 87 ± 24.4 g	23 23 23 23	Light sedation. Light sedation. Light sedation. Light sedation. Light sedation.	Davis, 2004 Davis, 2004 Davis, 2004 Davis, 2004 Davis, 2004

Table 14.1. (Continued)							
Class Osteichthyes Taxa	Drug	Dose	Route	Wt./Age	Temp (°C)	Comments	Ref.
Family Mugilidae Mugil cephalus (Grey Mullet) Myxus elongates (Sand Grey Mullet)	2-PE Clove oil in ethanol at ratio 1:5	400 mg/L 40 mg/L	<u> </u>	38.49 ± 3.85 g	31	Provided total loss of equilibrium allowing phlebotomy. Hseu, 1996 Induction within 3 min. Recovery within 5 min. Griffiths, 2 Sufficient for handling and measurement.	. Hseu, 1996 Griffiths, 2000
Family Mullidae Pseudupeneus maculates (Spotted Goatfish)	MS-222	30-50 mg/L	呂			Heavy sedation.	Neiffer, unpub.
Family Tripterygiidae Enneapterygius rufopileus (Redcap Triplefin)	Clove oil in ethanol at ratio 1:5	40 mg/L	Z		18	Induction within 3 min. Recovery within 10 min. Sufficient for handling and measurement.	Griffiths, 2000
Family Osphronemidae Colisa labiosus (Thick-lipped Gourami)	MS-222 buffered with NaHCO ₃	200 mg/L for induction. 80 mg/L for maintenance	Z	50 00		Induction: 90 sec. Total anesthesia time = 47 min. Flow rate of maintenance fluid = 12.1 ml/min. Gill motion throughout procedure. Full recovery by 23 min Surgical mass removal	Harms, 1995
Trichogaster trichopterus (Threespot Gourami)	MS-222 buffered with NaHCO ₃	400 mg/L	Z	$19 \pm 3 \mathrm{g}$	23-25	Induction within 2 min. Level sufficient for deep IM injection and phlebotomy. Recovery within 2 min. PA 7.6	Yanong, 2005
	Metomidate Quinaldine	60 mg/L 0.8 mg/L 5 mg/L			28-29 28-29 28-29	Level sufficient to induce light sedation within 4 min. Level sufficient to induce light sedation within 4 min. Level sufficient to induce light sedation within 4 min.	Crosby, 2006 Crosby, 2006 Crosby, 2006
Family Percidae Perca fluviatilis (European Perch)	Clove oil dissolved in 95% ethanol	6 mg/L	Z	17 g	15	Provided sedation for 6 hr without loss of equilibrium at which time fish removed from anesthetic.	Hoskonen, 2004
Perca flavescens (Yellow Perch)	Isoeugenol (AQUI-S)	20 mg/L	Z	Juveniles– young adults	12 ± 2	Induction within 3 min. Total exposure time ≤15 min. Recovery within 8 min. Useful for basic handling	Stehly, 1999
	Isoeugenol (AQUI-S)	$20~\mathrm{mg/L}$	Z	Fry-finger-lings 1.1 ± 0.22 g	12 ± 2	Induction within 4.1 min or less. Total exposure time ≤ 15 min. Recovery within 5 min. Useful for hatic handling procedures or $H = 8.1$	Stehly, 1999
Stizostedion vitreum (Walleye)	Isoeugenol (AQUI-S)	$50\mathrm{mg/L}$	Z	Juveniles– young adults	12 ± 2	Induction averaged 4.3 min. Total exposure time <15 min. Recovery within 8 min. Useful for basic handling angeddues, pH = 8.1	Stehly, 1999
	Isoeugenol (AQUI-S)	50 mg/L	呂	Fry-finger-lings 0.8 ± 0.16 g	12 ± 2	Induction averaged 3.9 min. Total exposure time <15 min. Recovery within 5 min. Useful for basic handling procedures. pH = 8.1	Stehly, 1999
Family Pomacanthidae Centropyge bicolor (Bicolor Angelfish)	MS-222	75 mg/L	Z			Sedation rated excellent. Diagnostic examination performed.	Neiffer, unpub.

Pomacanthus arcuatus (Gray Angelfish)	MS-222	50-100 mg/L	Z	0.2-1.7 kg	Provided mild to heavy sedation with a few animals considered lightly anesthetized at 100 mg/L. Diagnostic exams and topical treatments	Neiffer, unpub.
Pomacanthus paru (French Angelfish)	MS-222	50-80 mg/L	Z	0.40-1.95 kg	performed. $n = 16$ Provided mild to heavy sedation with a few animals considered excessively deep at 70–80 mg/L range.	Neiffer, unpub.
Pomacanthus semicirculatus (Koran Angelfish)	MS-222	1/8m S8-09	Z		Diagnostic examinations performed. $n=8$ Variable sedative effect (fair to excellent). Diagnostic exams and topical treatments performed. $n=2$	Neiffer, unpub.
Family Pomacentridae Abudefduf saxatilis	MS-222	100 mg/L	Z		Provided surgical anesthesia for kidney culture.	Neiffer, unpub.
(Sergeant Major) Amphiprion percula	MS-222	50-75 mg/L	Z		Provided mild to heavy sedation for examinations.	Neiffer, unpub.
(Percula Clownish) Chromis cyanea (Blue Chromis) Chromis multilineata	MS-222 MS-222	75 mg/L 75 mg/L	呂呂		Sedation rated as good. Examination performed. Sedation rated as good. Examination and transport.	Neiffer, unpub. Neiffer, unpub.
(Brown Chromis) Dascyllus melanurus	MS-222	30 mg/L	Z		Sedation rated as good. Diagnostic examination	Neiffer, unpub.
(Four Stripe Damseinsn) Dascyllus trimaculatus (Domino Damselfish)	MS-222	50-75 mg/L	Z		performed. Provided heavy sedation for examinations.	Neiffer, unpub.
Family Rachycentridae Rachycentron canadum (Cobia)	Medetomidine with Ketamine	0.122-0.240 mg/kg 6-13.5 mg/kg	\mathbb{M}	24-40 kg	Injected using spring-loaded pole syringe. Dose resulted in mild sedation. Supplemental dose of 0.100 mg/kg medetomidine and 2.8 mg/kg ketamine necessary for final capture. MS-222 at 50 mg/L has been used for maintenance during examinations, skin biopsies, and one enucleation. Reversal with atipamezole at 5× total mg dose of medetomidine given IM.	Neiffer, unpub.
Family Scaridae Scarus coelestinus	MS-222	75 mg/L	Z		Provided light anesthesia for diagnostic examination.	Neiffer, unpub.
(Midnight Parrothsh) Scarus guacamaia (Rainbow Parrotfish)	MS-222	50-75 mg/L	Z	2.03-7.45 kg	Effect varied from moderate sedation to light anesthesia. Diagnostic examinations	Neiffer, unpub.
Scarus vetula (Queen Parrotfish)	MS-222	50-75 mg/L	Z		performed. $n = 4$. Provided mild to heavy sedation. Diagnostic	Neiffer, unpub.
Sparisoma aurofrenatum (Redband Parrotfish)	MS-222	75 mg/L	Z		exammatons performed. Provided surgical anesthesia for enucleation.	Neiffer, unpub.
Family Sciaenidae Sciaenops ocellatus (Red Drum)	MS-222	80 mg/L	Z	26–27	Anesthesia induced in 2.5-6 min. Sufficient for	Thomas, 1991
	Metomidate	7 mg/L	Z	26-27	Anesthesia induced in 3-7 min. Sufficient for handling	Thomas, 1991
	Quinaldine sulfate	20 mg/L	Z	26–27	and priebotomy. $p_1 = 7.7 - 7.8$ Anesthesia induced in 2-4 min. Sufficient for handling and phlebotomy. $p_1 = 7.7 - 7.8$	Thomas, 1991

Class Osteichthyes Taxa	Drug	Dose	Route	Wt./Age	Temp (°C)	Comments	Ref.
Family Scombridae Sarda chiliensis (Bonito)	Ketamine plus Medetomidine Atipamezole	4 mg/kg 0.4 mg/kg 2 mg/kg	M	2.7 ± 0.6 kg	19.5-20.5	Injections placed in red lateral muscle, immediately ventral to the lateral ridge below the lateral line, posterior and dorsal to the end of the pectoral fin. Induction: 8.9 ± 2.1 min. Anesthesia time: 19.0 ± 3.8 min. Recovery following injection of atipamezole: 7.7 ± 8.5 min. Mortality in fish receiving atipamezole dose $<5 \times$ medetomidine	Williams, 2004
Scomber japonica (Pacific Mackerel)	Ketamine plus Medetomidine Atipamezole	53–228 mg/kg 0.6–4.2 mg/kg 5 × Medetomidine dose.	M M	0.33-0.40 kg	19.5-20.5	Injected placed in red lateral muscle, immediately ventral to the lateral ridge below the lateral line, posterior and dorsal to the end of the pectoral fin. Induction: 4–21min (mean = 9 min) for 37 fish; 45–56 min for 8 fish. Anesthesia time: 1–52 min (mean = 16 min). Recovery following atipamezole: 2–12 min (mean = 5 min), p.H = 7.8–7.9	Williams, 2004
Thunnus thynnus (Bluefin Tuna)	MS-222	90 mg/L	Z			Oxygenated water over gills at 12–20 L/min following induction until recovery. Minor surgical procedures, ultrasonographic examinations, and serial blood sampling	Sylvia, 1994
		75 mg/L	Z			Induction rapid and deep. For short procedures, fish captured and dosed in vinyl bag with supplemental oxygen provided. For longer procedures fish captured in stretcher and transferred to large pool containing MS-222. Once induced, fish transferred to exam table with oxygenated anesthetic water directed over gills. In either case, recovery involved directing anesthetic free water over gills until fish capable of forward swimming motion.	Cooper, 1994
Family Serranidae Epinephelus itajara (Goliath Grouper)	MS-222	75-95 mg/L	Z	7.7-106.2 kg		Provided mild to heavy sedation. Diagnostic examinations, injections, and topical treatments neglections $n = \xi$	Neiffer, unpub.
		95-125 mg/L	Z	3.4-10 kg		Effect variety from the size f	Neiffer, unpub.
Epinephelus polyphekadion	Clove Oil	$10\mathrm{mg/L}$	Z			(swill bracket surgeries and sampling), $n = 0$. Suitable for sampling and for transportation.	Afifi, 2001
(Camounage Grouper) Epinephelus morio (Red Grouper)	MS-222	80 mg/L	Z	0.51-8.64 kg		Effect ranged from mild sedation to light anesthesia.	Neiffer, unpub.
Mycteroperca bonaci	MS-222	80-100 mg/L	ZI	183-800 g		Examinations performed: $n - \lambda$. Provided adequate sedation for examination. $n = 5$.	Neiffer, unpub.
(pack Grouper) Wycteroperca venenosa (Yellowfin Grouper)	MS-222	50 mg/L	Z			Provided adequate sedation for examination.	Neiffer, unpub.
Family Siganidae Siganus lineatus (Rabbitfish)	Clove Oil	100 mg/L	Z	Juveniles 7–39 g	27–29	Time to anesthesia <3 min. Time to recovery <5 min. Suitable for examination. No mortality observed.	Soto, 1995

 Table 14.1.
 (Continued)

Table 14.1. (Continued)							
Class Osteichthyes Taxa	Drug	Dose	Route	Wt./Age	Temp (°C)	Comments	Ref.
	Quinaldine Sulfate (plus diazepam)	7.5 mg/L 1 mg/L	呂	Juveniles 6–7 g		Use for deep anesthesia, marking, handling and surgery. Induction: 0–1 min. Recovery: 3–5 min. Observations: opercular rate 170/min which is less than opercular rate observed when quinaldine sulfate is used alone to reach the same level of anesthesia Mortality. 0% nH = 7 9–8 2	
	Quinaldine Sulfate	10 mg/L	召	Juveniles 6–7 g		Light anesthesia achieved. Induction: 0–1 min. Recovery: 3–5 min. Observations: opercular rate 190/min. All fish remained sensitive to external stimuli. Mortality: 0% at light sedation dose, but 30%–100% at deep sedation dose of 15–20 mg/L. In these cases opercular rate increased to 190/min and then ceased. pH = 7.9–8.2	
Family Terapontidae Bidyanus bidyanus (Silver Perch)	Benzocaine Clove oil	20 mg/L 15 and 50 mg/L	Z Z	682 ± 99 g 682 + 99 g		Used for sedation during transport 15 mg/L sufficient for light handling, tagging, and harvesting (exposure time 60 min). 50 mg/L produced anesthesia suitable for surgical procedures	Kildea, 2004 Kildea, 2004
	Isoeugenol (AQUI-S)	15 mg/L	Z	682 + 99 g		(exposure time 30 min). Sufficient for light handling, tagging, and harvesting (exposure time 60 min).	Kildea, 2004
Family Zanclidae Zanclus cornutus (Moorish Idol)	MS-222	75 mg/L	Z			Sedation rated as excellent. Examination performed.	Neiffer, unpub.
Order Pleuronectiformes Family Paralichthyidae Paralichthys lethostigma (Southern Flounder)	MS-222	75 mg/L	呂			Provided adequate sedation for examination.	Neiffer, unpub.
Family Pleuronectidae Hippoglossus hippoglossus (Halibut)	MS-222	250 mg/L	Z	2915 + 592 g	9-10	Induction to anesthesia = 250–282 s. Dose allowed for handling and phlebotomy. Recovery time 495–649 s.	Malmstrøm, 1993
	Metomidate	20-30 mg/L	Z	$2915\pm592\mathrm{g}$	9-10	Induction to an esthesia = 189–310 s. Dose allowed for handling and allohologomy time 220, 220, 220, 220, 220, 220, 220, 220	\geq
		7/8m 6	Z	Age 12 mo	10.3 ± 0.5	nanding and priedotomy. Recovery time 220-320 s. Though times not given, induction considered rapid and recovery prolonged. Respiration was depressed. See information on same study results in turbot	. 1993 Hansen, 2003
		3 mg/kg (50 mg/ml soln. diluted with 0.9% NaCl to 3 mg/ml)	ΙΛ			(Scophthalmus maximus) in this table. No information on use, induction, or recovery, but good tissue distribution measured. No mortalities.	

Table 14.1.(Continued)

ng 10 min Hansen, 2003	tuar h and on- l.	min. balance/ tecovery If.	ery, but ortalities.		. Taylor, 1999	ed Graham, 1990 -300 s recovered	ole to be Harvey, 1987	surement, Woody, 2002 ery	ving Rothwell, 2005	Cho, 2000	Gilderhus, 1989 Jlight	Cho, 2000	Rothwell, 2005
Induction: 0.28–1.83 min. Recovery following 10 min	exposure: 19-56 min. Observations: opercular movement ceased 2.16-4.50 min into bath and resumed 0.63-2.98 min after placing in nonmedicated water. Heart rate was depressed. No mortality.	Induction: 2.5-5 min. Recovery time 11–35 min. Observations: Induction based on loss of balance/motor control and inability to right self. Recovery considered complete when fish righted self. No mortalities.	No information on use, induction, or recovery, but good tissue distribution measured. No mortalities.		Induction: 2.5–3.5 min. Exposed for 10 min. Recovery: 7.5–13 min. No mortality.	Injected into dorsal aorta via cannula. Caused immediate cessation of ventilation for 10–300 s with loss of equilibrium. Ventilation rate recovered within 1–2 hr	Sedation with partial loss of equilibrium. Able to be netted, but responsive.	Fish could be handled within 3 min for measurement, esophageal implants, and fin clips. Recovery within 10 min following 15 min exposure.	Resulted in light anesthesia. Recovery following 5 min exposure occurred within 5 min.	Provided deep anesthesia within 2 min.	Induction: 1–3.25 min. Recovery following 15 min exposure: 2.25–18.5 min. Provided light to heavy sedation.	Provided deep anesthesia within 2 min.	Sedation with partial loss of equilibrium. Suitable for handling.
18 ± 0.5						; 15		9-10	12.5 ± 2.5		7-17		12.5 ± 2.5
Age 8 mo		Age 8 mo, 228 g	Age 8 mo, 228 g		5.47-12.72 kg	$1.857 \pm 0.102 \text{ kg}$	2-3 kg	Adults	844-1,562 g	Juveniles $40.2 \pm 0.6 g$	Juveniles 80 g	Juveniles $40.2 + 0.6 \mathrm{g}$	844-1,562 g
Z		РО	2		Z	IS	IM	Z	Z	Z	Z	Z	Z
9 mg/L		7 mg/kg (concentration in a minced fish feed: cod liver oil emulsion delivered by	gavage. 3 mg/kg (50 mg/ml soln. diluted with 0.9% NaCl to 3 mg/ml)		25 mg/L	30 mg/kg	0.5-1.0 ml/kg	$50\mathrm{mg/L}$	100 mg/L with 300 mg/L NaHCO ₂	2(25–35 mg/L	$20\mathrm{mg/L}$	60 mg/L
Metomidate					Clove Oil	Ketamine	Alphaxalone– alphadolone (Saffon)	Clove oil	MS-222	MS-222 buffered 1:1 with NaHCO.	Benzocaine dissolved in ethanol at	Clove Oil in 1:10 ratio with 95% ethanol.	Isoeugenol (AQUI-S)
Family Scopthalmidae Scophthalmus maximus (Turbot)				Order Salmoniformes Family salmonidae	Oncorhynchus kisutch (Coho Salmon)			Oncorhynchus nerka (Sockeye Salmon)	Oncorhynchus tshawy tscha (Chinook Salmon)				

Table 14.1. (Continued)							
Class Osteichthyes Taxa	Drug	Dose	Route	Wt./Age	Temp (°C)	Comments	Ref.
	Isoeugenol (AQUI-S)	120 mg/L	곱	844-1,562 g	12.5 ± 2.5	Resulted in surgical anesthesia within 10 min for placement of vascular cannula. Recovery within 5–8 min	Rothwell, 2005
	Metomidate	42 mg/kg	IM	9 kg		Light sead to a straight partial loss of equilibrium.	Harvey, 1987
Oncorhynchus mykiss	Benzocaine	$20\mathrm{mg/L}$	Z	100-500 g	10	Provided adequate sedation within 30 s to permit	Oswald, 1978
(Rainbow Trout)	Benzocaine	25-40 mg/L	Z	Juveniles	7-17	weighing and injections. Induction: 1.25-5.5 min. Recovery following 15 min	Gilderhus, 1989
	dissolved in ethanol at 1 g /	30-45 mg/L		Z-500 g Adults 0.68–		exposure: 4–16 min. Provided light to heavy sedation. Induction: 2.25–4.5 min. Recovery following 15 min	:
	30 ml to make stock solution			2.04 kg		exposure: 5.5-13.5 min. Provided light to heavy sedation.	
	Clove Oil dissolved	2-5 mg/L	Z	Age 6 mo.	9.1 ± 0.2	Recommended for sedation suitable for 6-8 hr	Keene, 1998
	in ethanol at a ratio of 1:10	40-60 mg/L	Z	20.46 ± 0.73 g		transport. Provided deep anesthesia following 3–6 min exposure.	
	Isoeugenol	$20 \mathrm{mg/L}$	Z	Juveniles-	12 ± 2	Induction within 3 min. Total exposure time ≤ 15 min.	Stehly, 1999
	(AQUI-3)			young adults $754 \pm 145 \mathrm{g}$		Recovery within 8 min. Oserui for basic nandling procedures, pH = 8.1	
		20 mg/L	Z	Fry-finger-lings 4.1 ± 1.4 g		Induction within 4.1 min or less. Total exposure time ≤15 min. Recovery within 5 min. Useful for	
						basic handling procedures. $pH = 8.1$	
	Ketamine	50 mg/L	M	100-500 g	10	Induction generally within 5-10 min. Anesthesia persisted for 20 min at 130 mg/kg and 50-80 min	Oswald, 1978
						at 150 mg/kg. Apnea requiring assisted ventilation	
						occurred in 30% instit. Recovery took up to 30 inition and was characterized by excitement and ataxia.	
	Ketamine	30 mg/kg	V	$365 \pm 26 \mathrm{g}$		Injected into dorsal aorta via cannula. Caused	Graham, 1990
						immediate cessation of ventilation for 10-300 s	
						with loss of equilibrium. Ventilation rate recovered to pre-anesthesia values within 1–2 h.	
	Medetomidine	5-20 mg/L	Z	$300-400\mathrm{g}$	10 ± 0.2	Exposure for 10 min. Considered to be a good	Horsberg, 1999
	Atipamezole	30–80 mg/L	Z			sedative, but not anesthetic.	
		(0× Inedeto- midine dose)	N I			Exposed to aupaine for 7=10 mm. Exposure to 80 mg/L atipamezole resulted in panic-like reactions.	
	Alphaxalone-	130 and	ICo or	$100-500\mathrm{g}$	10	Induction within 5–10 min. Doses of 18 mg/kg	Oswald, 1978
	alphadolone (Saffan)	150 mg/kg	$^{2/_{3}}ICo + ^{1/_{3}}$			produced anesthesia. Lower doses only produced sedation. Recovery generally complete within 2 hrs.	
			M			Doses > 18 mg/kg associated with apnea and	
Salvelinus namavcush	Isoeugenol	20-50 mg/L	Z	Inveniles-	12 + 2	prolonged recoveries (3–6 hr). Induction in 2 5–3 9 min Total exposure time	Stehly 1999
(Lake Trout)	(AQUI-S)		, 1	young adult 167–1399 g	1	strain. Recovery within 8 min. Useful for basic handling procedures, pH = 8.1	
				0 , , , , , ,		marianta Presentation Presentation	

Salmo salar (Atlantic Salmon)	Benzoak (20% Benzocaine)	30-100 mg/L	Z	31-44 g	15	Provided sedation for 6 hrs without loss of equilibrium at which time fish removed from another. Considered useful for transport.	Hoskonen, 2004
	Clove oil dissolved in 95% ethanol	5 mg/L	Z	31-44 g	15	Provided sedation for 6 hrs without loss of equilibrium at which time fish removed from anesthetic. Considered useful for transport No mortality	Hoskonen, 2004
	Clove oil dissolved in 95% ethanol	8 mg/L	Z	1-yr-old smolts $44.7 \pm 12.8 g$	5.4 ± 0.2	Another a defined in 2.2–8.1 min. Exposure to 100 mg/L for >6 min may result in cessation of voluntary receives the contract of the contract o	Iversen, 2003
	Clove oil dissolved in ethanol	30-100 mg/L	Z	$\begin{array}{c} \text{1-yr-old smolts} \\ 44.7 + 12.8 g \end{array}$	5.4 ± 0.2	Anesthesia attained in 2.2–8.1 min. Exposure to 100 mg/L for >6 min may result in cessation of voluntary resoiration	Iversen, 2003
	Isoeugenol	30-100 mg/L	Z	1-yr-old smolts $44.7 + 12.8 \sigma$	5.4 ± 0.2	Anesthesia attained in 2.2–6.2 min.	Iversen, 2003
	Metomidate	2-10 mg/L	Z	1-yr-old smolts 44.7 + 12.8 g	5.4 ± 0.2	Anesthesia attained in 3.0–17.4 min. Exposure to 100 mg/L for >6 min may result in cessation of voluntary resultation	Iversen, 2003
Salmo trutta (Brown Trout)	Ketamine	130 and 150 mg/kg	M	100-500 g	10	Induction generally in 5–10 min. Anesthesia persisted for 20 min at 130 mg/kg and 50–80 min at 150 mg/kg. Apnea requiring assisted ventilation occurred in 30% fish. Recovery took up to 90 min and was characterized by excitement and ataxia	Oswald, 1978
	Alphaxalone- alphadolone (Saffan)	12-18 mg/kg	ICo or $\frac{2}{3}$ ICo $+ \frac{1}{3}$ IM	100-500 g	10	Induction within 5-10 min. Doses of 18 mg/kg produced anesthesia. Lower doses only produced sedation. Recovery generally complete within 2 hrs. Doses >18 mg/kg associated with apnea and	Oswald, 1978
Coregonus lavaretus (Whitefish)	Clove oil dissolved in 95% ethanol at 1:10 ratio.	3 mg/L	呂	31-44 g	15	Provided sedation for 6 hrs without loss of equilibrium at which time fish removed from anesthetic. Considered useful for transport. No mortality.	Hoskenen, 2004
Order Scorpaeniformes Family Anoplopomatidae Anoplopoma fimbria (Sablefish)	Metomidate	62 mg/kg	IM	3 kg		Light sedation with partial loss of equilibrium.	Harvey, 1987
	Alphaxalone- alphadolone (Saffan)	0.3–0.4 ml/kg (need mg)	IM	3-5 kg		Directed her avoidance. Light to heavy sedation with some fish exhibiting directed net avoidance. Recovery within 90 min.	Harvey, 1987
Family Sebastidae Sebastes caurinus (Conner Rockfish)	Metomidate	100 mg/kg	M	2 kg		Anesthesia with marked depression of ventilation. Recovery taking several hours.	Harvey, 1987
	Gallamine Triethiodide	1-4 mg/kg	IM	1–3 kg		Up to 2 hr until effect noted. Effect ranged from sedation (fish could be netted but were responsive) to anesthesia with marked depression of ventilation.	Harvey, 1987

Table 14.1. (Continued)							
Class Osteichthyes Taxa	Drug	Dose	Route	Wt./Age	Temp (°C)	Comments	Ref.
Family Scorpaenidae Pterois sp. (Dwarf Lionfish)	MS-222	75 mg/L	Z			Sedation rated as good. Diagnostic examinations	Neiffer, unpub.
Taenianotus triacanthus (Leaf Scorpionfish)	MS-222	50-90 mg/L	Z			Provided mild to good sedation. Diagnostic examination performed. $n = 3$.	Neiffer, unpub.
Order Siluriformes Family Clariidae Clarias gariepinus (North African Catfish)	Alphaxalone- alphadolone	24 mg/kg	M	Average 1,150 g	24	Pre–anesthetized by squirting a few ml of 2–PE on gills that induced almost immediate immobility. Once alphaxalone–alphadolone injected, the gills were rinsed with fresh water. Surgical anesthesia at 26 ± 8 min. Artificial respiration required by pumping gills. If the investigators assured that either the fish could reach the water surface from time to time during recovery or the fish were placed in shallow water (\leq 15 cm), the fish survived. If these precautions were not taken,	Peters, 2001
Family Ictaluridae (Ameiurus nebulosus) (Ictalurus nebulosus) (Brown Bullhead Catfish)	Alphaxalone- alphadolone	24 mg/kg	B	56-255 g	18	Injection given just behind first dorsal fin. Induction: within minutes. Gradually lost balance and eventually ventilation ceased. Artificial respiration required by pumping water over gills at ~ 100 ml/min. Surgical anesthesia required on average 20 min.	Peters, 2001
(-1			Š		Ç	inne until recovery of opercular movements averaged 207 min.	£000
Ameiurus melas (Ictualurus melas) (Black Bullhead Catfish)	Alphaxalone- alphadolone	24 mg/kg	\mathbb{Z}		18	Injection given just behind first dorsal fin. Event very similar to brown bullhead above	Peters, 2001
Ictalurus punctatus (Channel Catfish)	MS-222	100 mg/L	Z	Adult 1.1 + 0.04 kg	14.5	Anesthesia: 4.5 ± 0.8 min. Fish immediately transferred to anesthetic free water with recovery time of 1.7 ± 0.2 min. Survival 100% at 24 hrs. Dose considered useful for basic handling	Small, 2005
	Clove oil	100–150 mg/L (no ethanol used; water aerated strongly prior to addition of fish)	Inhalant	Inhalant Finger-lings $19.12 \pm 4.32 \text{ g}$	23	Induction: Within 1 min. Recovery: Following 10 min exposure to 100 mg/L, recovery occurred within 4 min. Recovery prolonged (>10 min) after exposure to 150 mg/L. Exposure to 100 mg/L for ≥ 20 min associated with increasing mortality. Exposure to 300 mg/L for 10 min resulted in 50%	Waterstrat, 1999
	Isoeugenol	2.5 mg/L	Z	Juveniles	26	Sedation arised in all fish. No mortality with	Small, 2004
	(AQUI-S)	40-60 mg/L	Z	Adult $1.1 \pm 0.04 \mathrm{kg}$	14.5	Time to an esthesia: 3.7–3.9 min. Fish immediately transferred to anesthetic free water with recovery time of 2.8–5.3 min. Survival 100% at 24 hrs. Dose considered useful for basic handling procedures.	Small, 2005

	Metomidate hydrochloride	6 mg/L	Z	Juvenile to adult 3–810 g	26	Induction: 0.46–2.31 min. Rapid recovery after 60 min exposure (2.01–2.52 min). Note: 65%	Small, 2003
	Metomidate hydrochloride	1.5 mg/L	Z	Juveniles $62 + 11.3 \mathrm{g}$	26	Sedation achieved in all fish. No mortality with exposure from 30 min to 24 hrs. pH = 8.6	Small, 2004
Family Pangasiidae Pangasius sp. (Pangasius Catfish)	Isoeugenol (AQUI-S)	20 mg/L	Z	Juvenile-young adults	12 ± 2	Induction in 5.3 min. Total exposure time ≤15 min. Recovery within 8 min. Useful for basic handling	Stehly, 1999
		20 mg/L	Z	$335 \pm 92.0 \mathrm{g}$ Fry-finger-lings $1.3 + 0.16 \mathrm{g}$		procedures, $pH = 8.1$ Induction within 4.1 min or less. Total exposure time ≤ 15 min. Recovery within 5 min. Useful for basic handling procedures, $pH = 8.1$	
Family Siluridae Kryptopterus bicirrhis (Glass catfish)	Alphaxalone- alphadolone	4.8 mg/L for induction 2.4 mg/L for maintenance	Z	Check on age, but likely adults 2–7 g	23-27	Opercular movements disappeared after 5 min exposure, at which time fish transferred to maintenance. Artificial respiration given by pumping water through mouth and across gills at $7-10$ ml/min. Recovery in ~ 30 minutes after being placed in clean water.	Peters, 2001
Order Tetraodontiformes Family Balistidae Canthidermis maculata (Rough Triggerfish)	MS-222	45-75 mg/L	Z			Provided mild to heavy sedation. Diagnostic examinations performed.	Neiffer, unpub.
Family Diodontidae Diodon holocanthus (Balloonfish) MS-222	MS-222	75-80 mg/L	Z	0.38-1.16 kg		Sedative effect rated fair to good. Diagnostic exams	Neiffer, unpub.
		100-125 mg/L	Z	0.38-0.42 kg		and topical treatments performed. $n = 3$. Provided surgical anesthesia for removal of fungal granulomas from integument and resection of	Neiffer, unpub.
Diodon hystrix (Porcupinefish)	MS-222	75-80 mg/L	Z			coelomic musculature. Mild to moderate sedation. Diagnostic examinations performed. $n = 2$.	Neiffer, unpub.
Family Monocanthidae Aluterus scriptus (Scrawled Filefish)	MS-222	50-60 mg/L	Z	0.44-2.35 kg		Sedation rated as good to excellent. Diagnostic examinations performed.	Neiffer, unpub.
Meuschenia trachylepis (Filefish)	Clove oil in ethanol	75–100 mg/L 40 mg/L	Z		18	Heavy sedation with cessation of gilling. Induction within 3 min. Recovery within 5 min.	Griffiths, 2000
Monacanthus tuckeri (Slender Filefish)	MS-222	$50\mathrm{mg/L}$	Z			Surrection of nationing and incapacitic Provided mild sedation. Diagnostic examination performed.	Neiffer, unpub.
Family Tetraodontidae Arothron nigropunctatus (Dogface Puffer)	MS-222	70-75 mg/L	Z			Provided mild to heavy sedation. Diagnostic examinations performed. $n = 3$.	Neiffer, unpub.
Sphoeroides testudineus (Checkered Puffer)	MS-222	100 mg/L 70–100 mg/L	<u> </u>	360 g 280-330 g		Provided surgical anesthesia for removal of skin lesion. Variable effect from mild sedation to light anesthesia. Examinations and topical laser surgeries performed. $n = 6$.	Neiffer, unpub. Neiffer, unpub.

ICo, intracoelomic; IM, intramuscular; IN, inhalant; IV, intravenous; MS-222, tricaine methanesulfonate; 2-PE, 2-phenoxyethanol; PO, orally. Where possible, the most recently accepted scientific name is used.

Regardless of available information, the anesthetic regimen for an untested species should be tried through to recovery using one or a small group of fish. Start at the low end of the recommended dosage range and work up to the desired effect (Harms, 1995; Ross and Ross, 2001; Stetter, 2001). However, in a species whose anesthetic tolerance is known use a high dosage for a smoother and more rapid induction. Once induced, a lower inhalant maintenance dosage is usually appropriate (Harms, 1999).

Pre-anesthetic Preparation

The following are preferably performed before induction:

- 1. Baseline behavioral parameters (i.e., ventilation, caudal fin stroke rate, and overall activity level) are recorded for comparison during anesthesia.
- 2. Although aspiration pneumonia is not a concern, it is not uncommon for fish to regurgitate material that clogs gill rakers and contributes to water quality degradation. Fasting for 12 to 24 hours (one feeding cycle) limits regurgitation and decreases nitrogenous waste production (Harms, 1995; Stetter, 2001).
- 3. Containers with adequate water for transportation, induction, maintenance, and recovery are prepared (Harms, 1999; Stetter, 2001). This is particularly important when water is used for inhalant anesthesia. If the procedure occurs next to the animal's tank, it can be used for recovery. This assumes monitoring is possible and other specimens will not traumatize or consume the fish during recovery.
- 4. The physical (e.g., temperature) and chemical (e.g., pH, salinity) variables of all water used are matched to those of the fish's source water. Dissolved oxygen is maintained greater than 5 ppm (mg/L) with 6 to 10 ppm ideal (Harms, 1999; Stetter, 2001).
- 5. For out-of-water procedures a plan is made for preventing drying of the skin, fins, and eyes. This can include coverage with clear plastic drapes and regular rinsing of tissues with water from a bulb syringe or a small portable atomizer (Harms, 1999; Ross and Ross, 2001).

Inhalant Anesthesia

Inhalant anesthesia is analogous to gaseous anesthesia in terrestrial animals. The anesthetic in solution is ventilated by the fish, enters the bloodstream through the gills \pm accessory respiratory organs \pm the skin and passes rapidly to the central nervous system. When returned to drug-free water, drugs or their metabolites are excreted mostly via the gills and presumably accessory respiratory organs. Some elimination also occurs through the kidneys and presumably the skin (Ross and Ross, 2001; Walsh and Pease, 2002). Unlike in terrestrial vertebrates, any water-soluble drugs or metabolites excreted from fish are continuously absorbed through

the body surface and gills, while being simultaneously metabolized and eliminated (Oikawa, Takeda, and Itazawa, 1994). This is problematic for assessing dosage effects and performing pharmokinetic studies unless flow-through systems or closed systems with inline carbon filters are used.

Inhalant drugs must be water soluble or use a water-soluble solvent as a vehicle. It is always preferable to use water from the fish's tank or pond to make the anaesthetic solution. For simple, short procedures the required drug concentration is made up in an aerated container to which fish are transferred or drugs are added directly to the water containing the fish. In the latter situation a buffer (e.g., sodium bicarbonate) is added prior to drug administration to minimize acute drops in pH (Harms, 1999; Ross and Ross, 2001). Ideally, spontaneous ventilation is maintained during short procedures.

For large fish, in which immersion is impractical or dangerous to handlers, drugs may be applied directly to the gills. Inexpensive plastic pump spray bottles are ideal for this application (Figure 14.1). When used by divers, the addition of a harmless dye (e.g., food coloring) helps identify distribution of the anaesthetic.

Regardless of application, anesthetic solutions are most accurately made using a measured volume of a standard stock solution. However, preparing stock solutions of expensive powdered anesthetic drugs (e.g., MS-222) is uneconomical if used infrequently because potency decreases over time (Ross and Ross, 2001). Alternatively, pre-weighed drug packets are recommended. Waterproof quick reference charts and known volume containers are useful for procedure set up. More

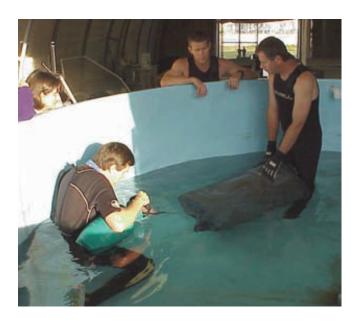


Figure 14.1. Large grouper (Family Serranidae) being anesthetized using a pump sprayer to deliver concentrated MS-222 into a retreat being used by the fish.

importantly, they enable quick modification of drug dosage level (Figure 14.2).

An artificial ventilation system is used for procedures lasting greater than 10 minutes, debilitated fish, species that are slow to recover, and all but the shortest out-of-water procedures. The animal is held in shallow water or placed on a fenestrated surface in lateral recumbency or upright/upside down in a foam holder. Aerated anesthetic solution is delivered across the gills from a bifurcated pipe or mouthpiece placed in the buccal cavity (Figure 14.3). Non-recirculating or recirculating system can be used. In its simplest form, a non-recirculating system uses an IV fluid bag and drip set. Resealable bags are easier for preparation, but use sealed bags with an opening cut in the end suffice (Figure 14.4). Flow rate is controlled by the drip set valve. Aeration of the



Figure 14.2. Use of waterproof dosage charts such as these for MS-222 along with pre-weighed drug packets and known volume containers enable quick modification of drug dosage level during procedures.



Figure 14.3. Goliath grouper (Epinephelus itajara) positioned in dorsal recumbency in a foam holder during anesthesia with MS-222. Note the bifurcated mouthpiece being placed in the buccal cavity for delivery of oxygenated anesthetic water to both sets of gill arches.

anesthetic water with an air stone in the IV bag ensures near-saturation of oxygen and removal of dissolved CO_2 . Used water is collected, but not recycled (Harms, 1999; Ross and Ross, 2001; Stetter, 2001). This system is suitable for small to medium-sized fish depending on reservoir volume, drip set tube diameter, and the rate at which fluid can be delivered.

Recirculating systems enable delivery of anesthetic water from a reservoir to the gills and recycling of the effluent back to the fish (Figure 14.5). This recycling is either done manually (refill elevated reservoir with collected effluent) or with a submersible pump. When using pumps, electrical safety for the operator is considered. Flow rate is controlled by a valve on the tube leading to the mouth. Minimum effective flow rate during fish anesthesia has not been determined; 1 to 3 L/minute per kg is recommended. Low delivery rates fail to keep the gills on both sides wet, reducing gas exchange. High flow rates result in alimentary anesthetic delivery and gastric dilatation. Oxygenation is provided as described. Recirculating systems are used in large fish where cost and waste water concerns make conservation of anesthetics and water paramount (Harms, 1999; Ross and Ross, 2001; Stetter, 2001).

Regardless of method used, drug concentration adjustment in response to anesthetic depth is difficult. One option is to prepare measured volumes of anesthetic-free water and concentrations of anesthetic



Figure 14.4. A simple non-recirculating system using a resealable intravenous bag and drip set. Sealed bags with an opening cut in the end will suffice. Gravity dependent flow rate is controlled by the drip set valve. Used water is collected, but not recycled. This system is suitable for small to medium-sized fish, depending on the volume of the reservoir, the drip set tube diameter, and the rate at which fluid can be delivered.



Figure 14.5. A grunt (Haemulon sp.) anesthetized with MS-222 and maintained using a simple recirculating system that enables delivery of anesthetic water from a reservoir to the gills and recycling of the effluent back to the fish by use of submersible pump.

solution. These solutions are placed in separate bags or reservoirs and used in either recirculating or non-recirculating systems. Alternatively, a syringe or turkey baster is used to rapidly deliver small amounts of fluid directly to the gills without disconnecting the fish from the system (Harms, 1999).

The flow is usually normograde to achieve optimal gas and anesthetic exchange. During oral surgery flow is reversed, if necessary, for surgical access. However, retrograde flow nullifies the normal countercurrent exchange mechanism and may damage the gills. The size or anatomy of some fish (e.g., filefish, Monocanthidae) (Figure 14.6) make placement of a bifurcated buccal tube difficult. In these species, some retrograde flow is used to ensure all gill tissue is adequately perfused.

Parenteral Anesthesia

In addition to inhalation, anesthetics are delivered orally, intravenously (IV), intramuscularly (IM), and intracoelomically (ICo). Oral administration is rarely used because precise dosing is difficult and the rate and degree of absorption are uncertain (Harms, 2003). However, a few examples of successful use of oral drugs exist (Harvey et al., 1987; Harms, 1995; Steers and Sherrill, 2001; Hansen, Nymoen, and Horsberg, 2003). Intravenous injection is the fastest delivery method with rapid induction and usually short duration of effect. However, this route has limited clinical use because it requires either manual restraint or prior administration of drugs by another route to allow IV access (Fleming et al., 2003; Hansen, Nymoen, and Horsberg, 2003).

Intramuscular is the most common parenteral route. ICo has an increased risk of visceral damage and drugs must pass through the serosal surface making induction



Figure 14.6. Normograde flow of water through the buccal cavity provides for optimal gas and anesthetic exchange. However, during oral surgery or owing to anatomical challenges such as seen with scrawled filefish (Aluterus scriptus), use of retrograde flow may be required. In these cases ventilation efficacy is decreased and there is potential for damage to gill filaments.

time erratic. Both IM and ICo routes are used in larger fish because many are kept in large volume aquariums or pens where adding water-borne anesthetics is impractical and because injection site trauma is less problematic in larger specimens (Harvey et al., 1987; Williams, Christiansen, and Nygren, 1988; Harms, 1999). In the author's experience, injected fish will stop swimming and begin to drop through the water column with or without obvious gilling. However, when approached by divers with a net they often arouse and swim with directed movement. The diver retreats and allows the drugs more time to act and/or supplemental drug injections are made. Regardless of ease of capture, parenteral anesthetics often do not provide adequate sedation or anesthesia and supplemental inhalation anesthesia is required. Ventilatory support is necessary during parenteral immobilization, particularly if recovery is prolonged (Harms, 1999).

Injections are made by hand syringe, pole syringe (Figure 14.7), or a darting system. Examples of darting systems include a modified Hawaiian sling, pneumatic spear guns, and a laser-aimed underwater gun (Harvey et al., 1987; Williams, Christiansen, and Nygren, 1988; Harms, 1999). The latter propels darts from a distance of 1 to 2 m (4 to 7 ft) that inject pneumatically upon impact and remain attached after jettisoning the lightweight spear shaft. Both barbless and barbed needles are used for large active and heavily scaled or sluggish fish,



Figure 14.7. Examples of pole syringe systems used for fish. The lower image is a commercially available spring loaded syringe capable of injecting 12 cc of solution. Corrosion when used in salt water is a concern. The upper image is a system fashioned out of two sections of PVC pipes. The larger provides stabilization, whereas the lower has been provided with an internal stop (cable ties) and holds a standard pressurized dart. A piece of duct tape holds the dart to the pipe. Filtered food dye has been added to the contents of the syringe so injection success can be judged.

respectively (Harvey et al., 1987). A complication of dart use is injection site trauma and scale loss, with some fish requiring local or systemic wound treatment. Intramuscular injections often result in leakage of some injected drug as the needle falls out or is withdrawn and the surrounding muscles contract (Harms, 1995; Peters et al., 2001). If the fish is in hand for injection, the needle is placed directly on dorsal midline between epaxial muscles, and then laterally inserted into a muscle bundle to reduce drug loss (Harms, 1995). The author sometimes adds filtered food dye to the contents of the syringe, so injection success can be judged. Alternatively fluorescein stain or methylene blue dye is used (Harvey et al., 1987).

A first consideration when using parenteral anesthetics is human safety. The large dosages and drug volumes required make accidental injection a possibility for handlers (Harvey et al., 1987).

Monitoring

Anesthetic Depth Various schemes are used to describe anesthetic depth in fish with no consensus (Oikawa, Takeda, and Itazawa, 1994; Myszkowski, Kamiński, and Wolnicki, 2003; Detar and Mattingly, 2004). This makes comparison of regimens between and within species difficult when reviewing the literature.

Common criteria used in defining anesthetic depth or level include activity, reactivity to stimuli, equilibrium (righting reflex), muscle tone, and respiratory and heart rates. Broad stages include sedation, narcosis or loss or equilibrium, and anesthesia, and each stage is subdivided further into light and deep planes (Stetter, 2001; Harms, 2003). Depending on the species, drug, and dosage used, some stage components are unrecognized (Harms, 1999; Stetter, 2001). Conversely, some signs

attributed to drug effect are instead responses to stress. For example, Gulf of Mexico sturgeon (*Acipenser oxyrin-chus de soti*) often turn into a ventral/dorsal position when stressed (Fleming et al., 2003). Therefore, loss of the righting reflex is not used to determine anesthetic stage in this species.

For most fish, induction occurs in 5 to 10 minutes with inhalant drugs, but can be prolonged using other routes. During induction swimming, respiratory rate and reaction to stimuli decrease. As the fish becomes anesthetized, there is loss of equilibrium and response to stimuli. At a surgical anesthetic plane, there is total loss of muscle tone and a further decrease, but not cessation, in respiratory rate. A firm squeeze at the base of the tail is used to determine response to stimuli; if the animal does not respond, general anesthesia has been obtained (Stetter, 2001; Harms, 2003). Some species go through excitement during inhalant induction and may traumatize themselves (Harms, 1999; Stetter, 2001). Fish exposed to high drug concentrations may exhibit rapid and repeated flaring of the opercula, with a "coughing" reflex to flush the chemical irritant from the branchial cavity. As will be discussed, some drugs that attain immobility are devoid of analgesic effects and should not be used for surgical or similarly noxious procedures.

Cardiopulmonary Respiratory and cardiac rate changes are useful in assessing anesthetic depth. Both usually decrease with increased anesthetic dosage and anaesthetic time. Respiratory rates are determined in the perianesthetic period by observing opercular movement (Harms, 1999, 2003; Stetter, 2001). However, in some species (e.g., scombrids) opercular movement is minimal to non-existent. Additionally, passage of oxygenated water over the gills of any anesthetized fish with ceased opercular movement maintains adequate ventilation, at least short term. This is accomplished because of the large differential between respiratory and cardiac arrest. The heart still supplies fresh arterial blood to the gills, allowing for adequate gas exchange.

In species with thin pliable body walls and proportionally large hearts, heart beats are observed directly, but for most it is neither visible nor palpable (Harms, 1995, 1999). In these species heart rate is monitored using cardiac ultrasonography, Doppler flow probes, or electrocardiography (Harms, 1995, 1999; Ross and Ross, 2001). During cardiac ultrasonography, the probe is placed into the opercular slit of medium to large fish, or directly over the heart in smaller or small scaled/scaleless species (Figure 14.8). Doppler probes are placed in the same locations (Figure 14.9). Regarding electrocardiogram, electrodes can be clamped lightly to the surface of the fins with the pectoral and anal fins being a good combination (Ross and Ross, 2001). Alternatively, subcutaneous placement of needle electrodes minimizes skin trauma, reduces the chance of grounding out the ECG signal by contact with a wet external surface,



Figure 14.8. Ultrasonography is a useful tool for monitoring heart rate in fish. In specimens of sufficient size, the probe can be placed into the opercular slit as in this rainbow parrotfish (Scarus quacamaia). Alternatively, the probe is placed directly over the heart in smaller specimens or small scaled/scaleless species.



Figure 14.9. Doppler flow is also used for monitoring heart rate in fish with probes placed as described for ultrasonography. This figure demonstrates placement of the probe into the opercular slit of an African cichlid (Protomelas insignis).

and improves signal quality (Harms, 1999). Pulse oximetry is not effective for measuring hemoglobin saturation in fish (Harms, 1999; Ross and Ross, 2001).

If the animal is stable, respiratory and heart rates are measured and recorded every 2 to 5 minutes. It is important to focus on trends because normal rates are not known for most species. Anesthetized fish generally have slower heart rates than terrestrial animals of similar size (Stetter, 2001).

Other variables that are visually or palpably monitored include equilibrium, jaw tone, color of fin margin (pallor = hypoxemia, hypotension or peripheral

vasoconstriction), response to touch or surgical stimuli, and gill color (pallor = hypoxemia, hypotension, hypovolemia or asystole) (Harms, 1995, 2001; Stetter, 2001).

An effective way to monitor respiratory efficiency is periodic blood gas sampling to determine oxygenation, carbon dioxide, and pH. Venous samples are easier to collect and useful information about physiological trends is obtained. Other blood variables used to assess metabolic status include HCT, glucose, and lactate. Small size or debilitation may preclude collection of even a single sample from some individuals.

Water Quality After cardiorespiratory function, water quality monitoring is critical to reducing anesthetic morbidity and mortality. Assuming aeration, DO, and temperature are appropriate and constant, ammonia concentration is of greatest concern. Ammonia concentrations will rise and buffering capacity will decrease during prolonged procedures and when multiple fish are sequentially anesthetized in the same system. More alkaline water pH, as in marine systems, enhances ammonia toxicity. Ammonia concentrations are easy to measure with tank side kits. Alternatively, the handler uses other indicators of deteriorating water quality (e.g., surface foam formation due to increased protein from fish slime) (Harms, 1999). Some species (e.g., Gulf toadfish, Opsanus beta) are facultatively ureotelic and ureogenic. In contrast to most teleosts that are obligate ammonioteles, the toadfish switches to ureotelism in response to moderate stressors (e.g., anesthesia) excreting the majority of its nitrogenous waste as urea (Gilmour et al., 1998). Consequently, ammonia level measurement as a guide to water quality is inaccurate for this and similar species.

Declining water quality during anesthesia is corrected with a partial water change. The handler either adds water containing a known anesthetic concentration or, when reducing anesthetic depth, a known volume of clean water to the system.

Recovery

Recovery from inhalant anesthesia occurs when the fish is placed in drug-free water (Ross and Ross, 2001). Although recovery is predominantly by different mechanisms, this is also done when oral or parenteral drugs have been used. Some of these drugs and their metabolites may be excreted into the water and be reabsorbed across the gills and/or skin. The recovery water is aerated with the fish's mouth oriented toward water flow. In an artificial ventilation system, clean drug-free water is passed over the gills until spontaneous ventilation returns. Alternatively, if the fish is not spontaneously ventilating it is pulled forward through the water with its mouth open. Dragging the animal backward through water may cause gill damage and is avoided. Most fish fully recover within 5 minutes from inhalant anesthetics. Recoveries extending greater than 10 minutes indicate either excessive anesthetic dosage or a medically compromised animal (Ross and Ross, 2001; Stetter, 2001). In comparison, recovery from oral and parenteral agents is often greater than 5 minutes. The time is dependent on route, rate of drug metabolism, and if a reversal agent is used. As the fish recovers, respirations increase, muscle tone returns, fin movements start, and the fish swims with progressively less ataxia until full equilibrium is regained. Some fish go through an erratic porpoising phase and are prevented from escaping from tank (Harms, 1999). Certain individuals may need to be manually restrained during this period to prevent damage to eyes and body.

Resuscitation

Marked hypoventilation or apnea is usually not alarming. If cardiac output is maintained and oxygenated water is flowing appropriately over the gills, tissue gas exchange is probably adequate. Decrease the anesthetic concentration or move the fish to anesthetic-free water until respirations resume (Stetter, 2001). If involved in a major procedure, the latter is not advisable. In either scenario, the anesthetist takes advantage of the "buccal flow/heart rate" reflex; increasing water flow through the buccal cavity accelerates heart rate. The subsequent increase in gill blood flow more rapidly eliminates inhalant drugs and hastens recovery. In emergencies, this is achieved in the recovery bath by gently moving the fish through the water in a forward direction. Once the fish begins to ventilate spontaneously, it is left to complete the process unattended (Ross and Ross, 2001). Unresponsive fish are given standard mammalian emergency drugs such as doxapram, corticosteroids, and fluids. The author has observed positive response to doxapram administration (5 mg/kg IV or ICo) in several cases of respiratory arrest. Controversy over the use of epinephrine versus norepinephrine in fish exists and is an area in need of further investigation.

ANESTHETIC DRUGS

General Comments

Of the definitions of anesthesia, the following is perhaps more acceptable given the controversy regarding pain perception in fish, "Anesthesia is a biological state induced by an external agent which results in the partial or complete loss of sensation or loss of voluntary neuromotor control through chemical or non-chemical means" (Bressler and Ron, 2004).

Rather than listing a few cross taxa dosage recommendations for several commonly used drugs, the author has taxonomically arranged cited and anecdotal dosages for representative species from most orders (Table 14.1). Some extrapolation is always necessary, but the more species-based data one can refer to, the more accurate the educated guess will be.

Inhalant (Water-borne or Immersion) Drugs

Tricaine Methane Sulfonate (MS-222) Tricaine methane sulfonate (MS-222) is a benzocaine derivative with a sulfonate radical, which accounts for its water solubility and increased acidity over the parent compound (Oikawa, Takeda, and Itazawa, 1994; Harms, 1999). It is absorbed across the gill epithelium (\pm skin) and biotransformed in liver and probably kidney. It is cleared primarily through the gills as free and acetylated forms, with additional metabolites eliminated in urine and bile (Harms, 1999). Tricaine powder is directly mixed into the anesthetic chamber or administered as a stock solution of 10 g/L (10,000 mg/L). The latter is unstable in light and is kept in a dark container. Oily residues in buffered stock solutions indicate the presence of a desulfonation product and decreased potency.

MS-222 is acidic and is more effective and safe in its neutralized form. Solutions are buffered to the pH of the holding water before immersing the fish. Although sodium bicarbonate is primarily used, other buffers include imidazole, sodium hydrogen phosphate, sodium hydroxide, and calcium carbonate. Exact amounts are measured out or the powdered buffer is incrementally mixed into the anesthesia chamber until the solid no longer dissolves and saturation is reached (Oikawa, Takeda, and Itazawa, 1994; Harms, 1999; Roubach, Gomes, and Val, 2001; Stetter, 2001).

MS-222 is not efficacious for all fish. For example, in Gulf of Mexico sturgeon it is minimally effective at providing immobilization at even 400 mg/L (4 to 10 times dosage used in most species). Slow induction and prolonged recovery times make this drug dangerous for use in wild caught sturgeon being released after examination (Fleming et al., 2003).

The margin of safety is narrower in young fish in warm, soft water, and there is species variation (Harms, 1999; Roubach, Gomes, and Val, 2001). In all age groups MS-222 can be associated with hypoxemia resulting from drug-induced hypoventilation (Oikawa, Takeda, and Itazawa, 1994; Harms, 1995; Davis and Griffin, 2004). MS-222 is a suspected carcinogen (Detar and Mattingly, 2004) and in fish and humans may cause reversible retinal deficits (Bernstein, Digre, and Creel, 1997; Sladky et al., 2001). A chronically exposed ichthyologist developed decreased vision, photophobia, and photopsia that resolved after terminating MS-222 contact for 7 mo (Bernstein, Digre, and Creel, 1997). Personnel with regular occupational exposure should wear gloves to prevent systemic absorption of this retinotoxic drug.

MS-222 is the only FDA-approved anesthetic for fish and, consequently, is widely used in United States aquaculture. However, there is a 21-day withdrawal period prior to human consumption or release to the wild. This makes its use impractical or incompatible with some farming operations and field work associated with fisheries data collection (Waterstrat, 1999; Sladky et al., 2001; Detar and Mattingly, 2004).

Benzocaine Benzocaine, the parent compound to MS-222, is similar in pharmacology, but is much less water soluble. Consequently, a stock solution in ethanol or acetone (100 g in 1 L) or propylene glycol is prepared prior to its use. The stock solution is kept in a dark bottle and held at room temperature (Harms, 1995; Iversen et al., 2003). Its relative insolubility may account for its usefulness in species sensitive to MS-222. For example, striped bass (*Morone saxatilis*) are very sensitive to MS-222, but are effectively anesthetized in benzocaine solutions (55 to 80 mg/L) (Hseu et al., 1998).

Other advantages include low toxicity to humans at the concentrations used and it can be removed from aquaculture facility effluents using activated carbon filtration. Even if not filtered, breakdown in water is approximately 4 hours, making it less likely to cause environmental contamination. Exposure also does not impair fish growth or reproductive capacity (Hseu et al., 1998; Gomes et al., 2001).

Efficacy and sensitivity to benzocaine is species and dosage related (Gomes et al., 2001) and it can stimulate the stress response as discussed previously. The only other major concern is its fat solubility that may result in prolonged recovery in older and gravid fish (Iversen et al., 2003).

Clove oil, Eugenol, Isoeugenol, and Aqui-STM Clove oil is a mixture of compounds, of which the phenolic eugenol comprises 85-95%. Isoeugenol and methyleugenol make up the remaining 5-15% of active ingredients. Commercially available clove oil has approximately 84% eugenol, but it is possible to purchase 100%. Clove oil and isoeugenol are "generally recognized as safe" (GRAS) by the FDA as a food additive for humans. Eugenol is similarly approved for use in animal feeds and is used in dental cement for temporary fillings (Harper, 2003). Aqui-STM contains primarily isoeugenol (Iversen et al., 2003; Kildea, Allan, and Kearney, 2004). Clove oil and/or Aqui-STM are approved as legal anesthetics with no withdrawal period in Australia, Chile, Finland, New Zealand, and the Faroe Islands (Hoskonen and Pirhonen, 2004), but neither clove oil, any component of clove oil, nor Aqui-STM is approved for use as a fish anesthetic in the United States (Stetter, 2001; Harper, 2003; Bressler and Ron, 2004; Davis and Griffin, 2004). Methyleugenol is carcinogenic in rodents making it unlikely clove oil use will receive FDA approval. However, Aqui-S and eugenol alone are under review by the FDA (Davis and Griffin, 2004).

Clove oil and eugenol are incompletely water soluble, particularly at cold temperatures. A 1:10 mixture of either in 95% ethanol yields a 100 mg/ml stock solution. Final concentrations of 40–120 mg/L are used for most species (the contribution of ethanol to the anesthetic effect is nil at these concentrations) (Harms, 2003).

In addition to use in aquaculture, research, and aquaria, clove oil is regularly employed in marine field

studies for sampling tide pool and tropical reef fish assemblages (Griffiths, 2000; Marnane, 2000; Ackerman and Bellwood, 2002). For tide pools, the volume is estimated and the drug is administered as in an anesthetic chamber. For reef surveys a section is covered with mesh net covered in turn by a nylon cloak. A solution of clove oil mixed with ethanol is then pumped into the netted area to temporarily immobilize all fish. Rotenone, an effective and non-selective ichthyocide, has historically been utilized for this purpose, but is more controversial given increasing conservation and environmental concerns (Ackerman and Bellwood, 2002). This application of clove oil may be of use in captive exhibits that often have elaborate rock or coral work making removal of fish for medical or maintenance reasons difficult.

Compared with other inhalant anesthetics, clove oil results in more rapid induction times and consistent anesthesia (Sladky et al., 2001; Bressler and Ron, 2004; Detar and Mattingly, 2004). However, isoeugenol (Aqui-S) is considered more effective (Ross and Ross, 2001). Although clove oil recoveries are also consistent, they are longer compared with other drugs (e.g., MS-222) (Sladky et al., 2001; Detar and Mattingly, 2004). Other claimed advantages include efficacy at a range of water temperatures, availability, lower expense, and handler safety (Bressler and Ron, 2004; Detar and Mattingly, 2004). As mentioned, the effect of clove oil and its components on the stress response is variable with suppression in some cases and activation in others. Unlike metomidate, the mechanism of action remains unknown (Small, 2005).

Although increased safety compared to other inhalant drugs has been claimed (Detar and Mattingly, 2004), a narrow safety margin compared with MS-222 has been reported (Sladky et al., 2001). In red pacu, most fish exposed to eugenol (100 mg/L) required resuscitation, and the risk of ventilatory failure increased with increasing dosages. An explanation for ventilatory failure and medullary collapse in some fish is a neurotoxic or hepatotoxic effect similar to those described in mammals (Sladky et al., 2001). Alternatively, it may be a function of the physical properties of eugenol oil or increased duration of exposure. As an oil, eugenol coats anatomic structures and its persistence on gill epithelia may block gaseous diffusion (Sladky et al., 2001). In addition, mild gill necrosis due to repeated exposure to low dose eugenol (9 mg/L) has been reported (Afifi, Al-Thobaiti, and Rasem, 2001). Along with safety concerns, some fish are very sensitive to small increases in concentration, acutely losing equilibrium. This is a problem when controlling concentrations in large tanks and clove oil and its components may not be suitable as transport drugs in sensitive species (Hoskonen and Pirhonen, 2004).

Although the analgesic effects of eugenol in humans result from the inhibition of prostaglandin H synthase (Keene et al., 1998), proof of analgesia in fish does not

exist (Sladky et al., 2001). In red pacu, fish anesthetized with eugenol were more likely to react to a hypodermic needle puncture than fish anesthetized with tricaine methanesulfonate raising the question of appropriateness of clove oil or related compounds for invasive or markedly noxious procedures.

Metomidate Metomidate is a non-barbiturate imidazole. Available in Canada under the trade name Marinil, it is not licensed in the United States, but is available for investigational use (Harms, 1999). It is readily water soluble and is stored in tight light protected containers. In addition to inhalation, the drug can be given orally (Harvey et al., 1987; Hansen, Nymoen, and Horsberg, 2003).

Metomidate suppresses cortisol response to anesthesia. It blocks adrenocorticotropic hormone stimulation of steroidogenesis, even when exogenous ACTH is injected intracoelomically. This occurs by a direct effect on the interrenal gland and the mitochondrial cytochrome P₄₅₀-dependent enzymes that catalyze the synthesis of cortisol (Iversen et al., 2003; Davis and Griffin, 2004; Small, 2005). Cortisol synthesis blockade may cause the anesthetized fish to transiently turn very dark. This may be because of reduced cortisol production terminating the negative feedback loop on ACTH synthesis. As ACTH synthesis is linked to melanocytestimulating hormone production, both compounds increase with the associated color change occurring (Harms, 1995, 1999).

In addition to sedation and anesthesia for minor procedures, metomidate is useful for limiting transport trauma. Fish transported while immobilized are damaged by contact with the container sides and bottom. Metomidate dosages that suppress the cortisol stress response still allow maintenance of equilibrium (Harms, 1999; Davis and Griffin, 2004).

Metomidate is a hypnotic, inducing sleep rather than general anesthesia. This is reflected in maintenance of opercular respiration for two times as long at the effective concentration as other inhalants (Mattson and Riple, 1989). Additionally, muscle fasciculations occur at low dosages indicating incomplete relaxation (Harms, 1999). Metomidate is probably a poor analgesic and should not be used alone for major surgical or noxious procedures (Harms, 1999; Hansen, Nymoen, and Horsberg, 2003).

In some marine species, metomidate has a wider therapeutic range compared to benzocaine (Hansen, Nymoen, and Horsberg, 2003). Among freshwater tropical fish, gouramis are very sensitive to metomidate and its use in cichlids (Cichlidae) in water of pH less than 5 is contraindicated (Harms, 1999).

Quinaldine and Quinaldine Sulfate Quinaldine sulfate (QS) is a strongly acidic, highly water-soluble powder that must be buffered. Rather than adding powder

directly to the water, QS is administered as a stock solution (10 g/L). Its parent compound, Quinaldine, is a yellowish oily liquid and must be dissolved in acetone or alcohol prior to mixing in water. Due to high lipid solubility, quinaldine tends to accumulate in the brain more than QS (Hseu et al., 1998; Harms, 1999; Ross and Ross, 2001). Like MS-222 and most inhalants, quinaldine and QS depress the central nervous system sensory centers. Unlike MS-222, neither drug is metabolized by fish and is excreted entirely unchanged (Hseu et al., 1998; Harms, 1999).

Although not approved for use in the United States (Harms, 1999), QS is common in aquaculture elsewhere because of its relatively low cost. This has also made quinaldine a popular tool for collection of fishes from tidal pools and small lagoons (Ross, 1984). Other reported advantages include effectiveness at very low concentrations, purported low toxicity and wide safety margin, and short fish recovery time (Kumlu and Yanar, 1999).

Despite claims of safety, mortality occurs in some species. For example, in gilthead seabream, low dosage QS (15–20 mg/L) resulted in 30–100% mortality (Kumlu and Yanar, 1999). In addition, quinaldine can be an irritant and has caused corneal damage in salmonids (Ross, 1984; Harms, 1995). Also of importance are studies that demonstrate that fish exposed to quinaldine or QS alone retain a strong reflex response to being touched, even when they have totally lost equilibrium and are deeply anesthetized. This, along with the potential lack of analgesia, make them inappropriate for transportation, handling, and surgical or similarly noxious procedures (Cullen, 1996; Harms, 1999; Kumlu and Yanar, 1999).

To reduce toxicity, and increase efficacy and analgesia, some researches have combined diazepam with QS. As demonstrated in gilthead seabream and sea bass (*Dicentrarchus labrax*), addition of diazepam to the QS bath results in fish entering a deeper anesthetic plane at lower QS dosages. This occurs with lower to no mortality, improved muscle relaxation, and reduced excitement in confined spaces (e.g., transport boxes) (Kumlu and Yanar, 1999; Yanar and Kumlu, 2001). Non-depolarizing neuromuscular blocking agents (gallamine triethiodide, tubocurarine chloride, and pancuronium bromide) IM eliminate the reflex responses in fish anesthetized by quinaldine alone (Kumlu and Yanar, 1999). However, these combinations do not provide analgesia.

2-Phenoxyethanol 2-Phenoxyethanol (2-PE) is a clear or straw-colored oily liquid. It has a faintly aromatic odor and is moderately water soluble. 2-PE was used initially in aquaculture to treat ichthyophoniasis and other fungal, bacterial, and parasitic diseases. Less expensive than many anesthetics, 2-PE has been widely used for sedation, particularly in fish transportation, as well as general anesthesia (Hseu et al., 1996, 1997; Ross and

Ross, 2001). Another advantage is that it causes no pH change when added to sea water (Hseu et al., 1998).

2-PE produces hypoventilation and has poor analgesia (Oswald, 1978). Also, sustained and regular exposure to 2-PE solution causes a neuropsychological syndrome in some handlers (Hseu et al., 1998).

Isoflurane There are limited published studies evaluating chlorofluorocarbon based anesthetics in fish, and care is exercised in their use. Isoflurane is considered safe and effective in freshwater and marine fish at concentrations ranging from 0.4 cc to 0.75 cc isoflurane/l H₂O for induction and 0.25 cc isoflurane/L H₂O for maintenance (Stetter, 2001). Isoflurane liquid is vaporized and bubbled through the water or is directly added to the anesthetic chamber. The latter involves spraying the drug through a 25-g needle beneath the surface of the anesthetic chamber. This allows small drug droplets to be distributed in the water (Stetter, 2001). Anesthetic depth is difficult to control and, because of insolubility in water, localized areas of higher concentrations may occur, resulting in overdosage. In addition, volatilization and difficulty in scavenging waste gas is a hazard to personnel (Harms, 1999; Ross and Ross, 2001). This is addressed, to some extent, by attaching a funnel system to a standard scavenging system and placing it immediately above the anesthetic chamber (Stetter, 2001). Given the disadvantages associated with its use, a number of researchers and clinicians recommend use of isoflurane or similar drugs only as a last resort anesthetic, for euthanasia, or not at all (Harms, 1999; Ross and Ross, 2001).

Carbon Dioxide Carbon dioxide for immobilization is obtained from three sources: CO_2 gas, sodium bicarbonate (NaHCO₃), or carbonic acid (H₂CO₃) (Prince, Low, and Lissimore, 1995; Gelwicks and Zafft, 1998). Use of carbon dioxide gas involves diffusing compressed CO_2 gas through air stones into water. The NaHCO₃ (baking soda) method involves mixing a specific amount of the drug with water to release CO_2 . Carbonic acid immobilization involves mixing equal volumes of sulfuric acid (H₂SO₄) and NaHCO₃ solutions in water to form carbonic acid and liberate CO_2 (Prince, Low, and Lissimore, 1995; Gelwicks and Zafft, 1998).

Carbon dioxide gas and NaHCO₃ methods are popular, but cumbersome for many field applications (Prince, Low, and Lissimore, 1995; Gelwicks and Zafft, 1998). In comparison, the materials needed for carbonic acid immobilization are compact and concentrations are easily controlled making it more applicable to field work (Gelwicks and Zafft, 1998). The carbonic acid method has its own disadvantage in that NaHCO₃ and H₂SO₄ solutions are designed to react completely and accuracy is essential. If one solution is mixed incorrectly, water chemistry (i.e., pH) will be significantly affected. Safe

handling of concentrated H₂SO₄ requires protective gloves, clothing, and glasses and work under a fume hood (Gelwicks and Zafft, 1998). The acid is added to the water, not the reverse.

Regardless of method, CO₂ use has many disadvantages. Concentrations in water are difficult to control and oxygen must be maintained at high levels. Blood gases and acid-base balance are markedly altered (Prince, Low, and Lissimore, 1995; Harms, 1999). To address the latter concern, some handlers use NaHCO₃ with CO₂ gas for its buffering effect (Prince, Low, and Lissimore, 1995). Alternatively, some handlers mix NaHCO₃ with glacial acetic acid to yield carbon dioxide concentrations sufficient for immobilization while limiting acid-base shifts (Prince, Low, and Lissimore, 1995).

Following immersion in water with a high CO₂ concentration, there is a rapid decrease in blood pH and increase in blood CO₂ concentration. Low blood pH results in less efficient oxygen transport to tissues, including the brain. The resulting cerebral hypoxia causes an overall inhibition of spontaneous activity of the CNS and the observed "anesthetic" effect (Harms, 1995; Gelwicks and Zafft, 1998). When fish are returned to freshwater, CO₂ diffuses out of the gills, blood pH rapidly returns to normal levels and fish recover. One may expect these changes in blood pH and subsequent cerebral hypoxia to produce morbidity. However, rainbow trout appear tolerant of these changes in blood pH. Recent studies provide conflicting evidence regarding effectiveness and safety of carbonic acid (Gelwicks and Zafft, 1998).

Although touted to decrease the stress response, CO_2 has questionable analgesia (Prince, Low, and Lissimore, 1995; Ross and Ross, 2001) and is not appropriate for invasive procedures.

In the United States the primary advantage of using CO_2 is that it is "generally regarded as safe, and there are not restrictions on its use which is appealing to both aquaculture and field work" (Gelwicks and Zafft, 1998; Harms, 1999). However, many handlers feel it should be used for immobilization or euthanasia as a last resort (Harms, 1999).

Oral Anesthetics

Metomidate In addition to being used as an inhalant, metomidate has been administered orally by high pressure syringe as a supplement in fish partially immobilized by remote injection (Harvey et al., 1987) and to turbot (*Scophthalmus maximus*) via stomach tube for rapid and complete immobilization (Hansen, Nymoen, and Horsberg, 2003).

Diazepam In addition to being combined with QS for inhalant anesthesia, diazepam-impregnated pellets have been fed to American shad (*Alosa sapidissima*), resulting in a slow anesthetic induction (Harms, 1995).

Tiletamine-zolazepam Although designed to be used as an injectable drug combination, successful sedation and translocation of greater than 70% of a population of captive yellowtail jacks (*Seriola lalandi*) was performed using tiletamine-zolazepam powder packed in gelatin capsules placed in food items. Mortalities were attributed to anesthetic overdosage from fish consuming more than one medicated food item (Steers and Sherrill, 2001).

Injectable Anesthetics

Ketamine Hydrochloride Ketamine is used alone or in combination with α_2 -agonists (Harms, 1999). Intramuscular injection is the most common route and requires high dosages in teleosts and sturgeons when used alone (Williams, Christiansen, and Nygren, 1988; Bruecker and Graham, 1993; Fleming et al., 2003). When available in the lyophilized form, a concentrated solution permitting a smaller volume IM injection can be prepared (Oswald, 1978). IV administration, although rarely reported, uses dosages one-third to onehalf of those used IM. Ketamine has been used for capture and manipulation of a number of marine and freshwater species (Williams, Christiansen, and Nygren, 1988) and for short duration procedures and transport (Oswald, 1978; Bruecker and Graham, 1993). Ketamine IV in coho salmon (Oncorhynchus kisutch), rainbow trout, and Midas cichlids (Heros citrinellum) reduces the oxygen demand during handling (Oswald, 1978; Bruecker and Graham, 1993).

Regardless of administration route, ketamine alone has a species specific effect in fish often characterized by incomplete anesthesia, periods of apnea, and prolonged recovery with excitement when used (Oswald, 1978; Graham and Iwama, 1990; Bruecker and Graham, 1993). To reduce dosage and apnea, and improve anesthesia, ketamine is often combined with the reversible α_2 adrenergic agonist, medetomidine. This combination provides safe and effective anesthesia in some species (Williams, Rollins, and Block, 2004), but respiratory depression, bradycardia (Fleming et al., 2003) and incomplete immobilization is noted in others. For the latter reason, either ketamine or a ketamine/medetomidine (K/M) combination is more appropriate as an aid to restraint rather than a substitute for inhalant anesthesia during major procedures. The author has found K/M particularly useful in capture of fish from large volume aquaria. Following sedation or slowing down with K/M, staff are able to net the fish and transfer them to an MS-222 bath for maintenance and evaluation.

Medetomidine Medetomidine is usually combined with ketamine and reversed with atipamezole. However, it can be used alone as an inhalant in rainbow trout to produce sedation, but not analgesia. Bradypnea was observed during immobilization with an increase in

respiration occurring after addition of atipamezole to the recovery water at 6 times the medetomidine concentration (Horsberg, Burka, and Tasker, 1999).

Xylazine In rainbow and brown trout, the lowest effective dose of xylazine (100 mg/kg) consistently produced apnea. Convulsant activity occurred during induction and recovery making it difficult to ensure artificial ventilation because the convulsions frequently dislodged the water supply. In addition, gross ECG disturbances were detected. Consequently, xylazine is not recommended in salmonids (Oswald, 1978). Given the proven usefulness of medetomidine in other teleost species, xylazine is not the preferred α_2 -agonist for any fish.

Propofol Propofol IV has been used successfully for rapid induction in Gulf of Mexico sturgeon, but caused significant respiratory depression. This complication was addressed by passing oxygenated water across gills. In addition to respiratory depression, uncomplicated bradycardia was noted (Fleming et al., 2003). At the author's facility, propofol in an African lungfish (*Protopterus annectens*) was associated with mortality. It is not certain if this was directly drug related or caused by an obligate air-breathing fish being recovered in water that was too deep to allow surface access.

Alfaxalone-alfadolone A combination steroid anesthetic, alfaxalone/alfadolone (A/A) mainly depresses central nervous system activity while leaving the integumentary sensory system operational. This makes it very valuable for research in sensory physiology, including mechanoreceptors (Peters et al., 2001). An advantage of A/A is its cardiac chronotropic and inotropic stimulatory effect with vasodilation of the gill capillaries. This seems to ensure adequate oxygenation of the blood compared with many other anesthetics (Oswald, 1978). As with all drugs, species differences are seen. In a collection of marine and freshwater species A/A was effective, but not consistent for capture of free swimming individuals (Harvey et al., 1987). In several catfish species A/A provided surgical anesthesia lasting several hours (Peters et al., 2001). In rainbow and brown trout, A/A produces similar long sleep times, but it is difficult to give a dose that simultaneously abolishes locomotion yet preserves ventilation (Oswald, 1978).

Lidocaine Lidocaine yields variable results as an immersion anesthetic. However, it is effective as an injectable local anesthetic in fish, alone or in combination with other drugs (Harms, 1995).

Miscellaneous Drugs

Gallamine triethiodide IM has been used for capture and handling of large tank fish, providing a smooth induction of paralysis following injection (Harvey et al., 1987). It is worth considering for non-invasive procedures or as an adjunct to anesthetic agents. A combination of etorphine-acetylpromazine (Large Animal Immobilon) has been used in trout for anesthesia, but given the human accidental exposure risks (Oswald, 1978) and availability of other agents, its use is not recommended. Ethanol is an inhalant anesthetic of last resort. Anesthetic depth is variable and difficult to control. However, in non-clinical situations or for euthanasia ethanol is sometimes available when other drugs are not (Harms, 1995).

ANALGESIA

Most sources define analgesia as the absence of pain in the presence of stimuli that normally would be painful without the loss of consciousness. The less used definition seems more universally acceptable as it includes absence of noxious stimulation as well as pain in the definition (Blood and Studdert, 1988; Thurmon, Tranquilli, and Benson, 1996). Putting aside the question of pain perception, fish have μ and κ opiate receptors throughout the brain, making it reasonable to expect some effect of opioid treatments in fish experiencing noxious stimuli (Harms et al., 2005).

Despite increased interest, limited information on the use of analgesics in fish exists. In one of the earliest studies, the lips of juvenile rainbow trout were injected with 0.1 ml acetic acid. This resulted in a marked increase in opercular rate compared with controls, and anomalous behaviors, including rocking from side to side and lip rubbing against the gravel and tank sides. Administration of high morphine dosages significantly reduced the opercular rate and the noxious stimulusrelated behaviors. These fish also returned to normal eating behavior faster. Thus morphine appears to act as an analgesic or at least antinociceptive in this and presumably other teleost fish (Sneddon, 2003). In a later study koi carp (Cyprinus carpio) underwent exploratory celiotomy and were treated with butorphanol, ketoprofen, or saline. Only koi injected with butorphanol exhibited no significant differences between pre- and postsurgery caudal fin beat frequency and vertical position in the water column. This suggests a mild behavioral sparing effect compared with the ketoprofentreated and saline control groups (Harms et al., 2005). Fish can become tolerant of morphine and naloxone reduces its effects (and presumably butorphanol) (Rose, 2002). Putting aside the pain perception controversy, it appears that analgesic drugs have application in reducing stress associated with noxious stimuli in teleosts and presumably other boney fish.

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15 Elasmobranchs (Sharks, Rays, and Skates)

M. Andrew Stamper

INTRODUCTION

Elasmobranchs (sharks, skates, and rays) are within the class Chondrichthyes (cartilaginous fishes), which also includes the holocephalans (chimaeras and elephant fish). According to Compagno (1999), there are approximately 60 families, 185 genera, and 929 to 1,164 elasmobranch species. With such a variety of animals, anesthesia can be challenging. However, experience has led to some generalities that can be applied to facilitate immobilization and anesthesia. Appropriate anesthetic regimens should be used when handling stressed fish or performing invasive sampling or surgery. Much of the information for safe and effective anesthetic procedures is anecdotal. This is further complicated by the variety of species, their adaptations to the environments in which they live, and their physiological state in the perianesthetic period.

VARIATION IN DRUG EFFECT

The response to a drug is dependent on many factors, including body temperature, hepatic biotransformation, renal function, drug receptor type and distribution, and the injection site.

Most elasmobranchs are poikilothermic, but some (e.g., porbeagle, *Lamna nasus*; mako, *Isurus oxyrinchus*; and white shark, *Carcharodon carcharias*) do have some endothermic abilities. Mako and porbeagle shark brain temperatures approach 6°C above ambient at 12°C, and these elevated temperatures are also measured in the eye, red muscle, and parts of the liver, stomach, and spiral valve (Muñoz-Chápuli, 1999). Body temperature determines enzyme activity and, thus, influences drug elimination and duration of effect.

Liver size and composition is species dependent. It can account for up to 23% of body weight and much (less than or equal to 80%) may be lipid (Holmgren and Nilsson, 1999). The amount of hepatic

cellular exposure, as well as lipid, influences drug pharmacodynamics.

The kidney is very different to that of mammals, having a higher filtration rate and different selectivity (Lacy and Reale, 1999). These differences may influence drug elimination rates. The elasmobranch renal-portal system allows blood from the caudal half of the animal to drain directly into the kidneys. This theoretically may enhance the nephrotoxicity or renal excretion of drugs. However, a study in box turtles, which also possess a renal portal system, suggests this potential risk is not clinically significant (Beck et al., 1995). At this time, the physiological impact of this design is not known in elasmobranchs.

The use of mammalian anesthetic drugs in elasmobranchs may result in several possible outcomes: (1) they may bind to the same active binding site and produce the desired effect; (2) the binding site may be slightly different or there may be a lower number of binding sites, resulting in a weakened response; (3) there may be no binding sites at all, resulting in no effect; or (4) there may be a chemically similar binding site but one that triggers a different physiological function, resulting in a completely different response. Drugs can also bind with blood proteins or other non-target tissue, thus altering the amount of drug available and the effect on target tissue.

Drug response is somewhat determined by the injection site. Some species have regional heterothermy (Totland et al., 1981; Bernal and Graham, 2001) associated with a variable vascular density that may result in unpredictable drug uptake.

Other factors that may influence drug response include gill surface area to body weight ratio; lipid content; stress; health status; and body condition changes associated with age, season, sexual maturity, and nutrition. Therefore, many variables need to be considered when anesthetizing elasmobranchs. This may be the reason for the wide variety of reported responses to anesthetic regimens.

MONITORING

In captive animals a quiet environment without predatory tank mates should be used for anesthetic induction and maintenance. Several baseline physiological variables should be monitored. Ventilation rates are recorded if the animal is actively pumping water through the gills and not ram-ventilating (i.e., using forward motion to force water through the gills). Caudal fin strokes are measured to determine the onset of drug effect; this activity is usually the first to be reduced. Anesthetic stages in elasmobranchs are similar to mammals. However, the period between respiratory and cardiac arrest is greater because the respiratory capillaries are able to exchange oxygen and carbon dioxide when water flow over the gills is maintained with a pump. Further, anesthetic levels are highly variable between different animals (both intraspecies and interspecies) and drugs.

After an animal becomes ventrally recumbent respiration and righting reflex should be closely monitored. If respiration ceases, heart rate is monitored using either an ultrasound or Doppler flow detection probe placed over the heart, which is found ventral midline just caudal to the gill openings.

If the animal is stable, cardiopulmonary variables are monitored every 2 to 5 minutes and any trends identified. Although animals may appear to be ventilating well, bradycardia and an increased resistance to gill capillary flow (as erythrocytes accumulate within the capillary bed and become swollen) has been noted to possibly cause hypoxemia (Tyler and Hawkins, 1981). Respiratory effectiveness can be assessed with periodic blood gas analysis to determine oxygenation, carbon dioxide, pH, and lactic acid levels. Experiments with larger spotted dogfish (Scyliorhinus stellaris) indicated that CO₂ pressure in arterial blood was increased immediately after exercise, but returned to baseline within 1 hour. The pH gradually decreased, reaching a minimum in the second hour and returning to baseline within 8 hours. Lactate concentrations increased slowly to very high levels, reaching a maximum of 220 mg% within 6 to 8 hours after exercise (Piiper and Bumgartner, 1969). Since arterial samples are very difficult to obtain from sharks, venous samples are used to determine trends. Hand-held analyzers are relatively expensive, but offer rapid analysis at poolside or on a boat and many automatically adjust calculations for lower body temperature. Further investigation is needed to determine whether lactate levels indicate an animal is at increased risk for morbidity and mortality.

PHYSICAL RESTRAINT

Tonic immobility or hypnosis is induced by placing an animal in dorsal recumbency. It has been reported in a variety of elasmobranchs, including the clearnose skate

(Raja eglanteria), cownose ray (Rhinoptera bonasus), southern stingray (Dasyatis americana), blacktip reef shark (Carcharhinus melanopterus), Caribbean reef shark (Carcharhinus perezi), leopard shark (Triakis semifasciata), swellshark (Cephaloscyllium ventriosum), whitetip reef shark (Triaenodon obesus), and shovelnose guitarfish (Rhinobatos lentiginosus) (Henningsen, 1994). The level of restraint and duration of effect are highly variable between species. Restraint is often accomplished after a period of marked excitement, especially in batoid species.

CHEMICAL IMMOBILIZATION

Immersion Anesthesia

This technique has the advantage of being relatively safe to deliver and it can be modified by addition or dilution of the solution. A major disadvantage is the large amount of drug needed to accomplish immobilization, especially with large elasmobranchs. Further, the use of immersion drugs in large bodies of water is usually not practical or economically feasible.

Benzocaine Benzocaine is similar in action to MS-222, but is much less water soluble unless dissolved in acetone or ethanol. Its advantages include high potency, quick onset of effect, high safety margin, and relatively low cost (Larid and Oswald, 1975; Tyler and Hawkins, 1981). As with MS-222, Tyler and Hawkins (1981) report physiological changes most likely caused by hypoxemia from anesthetic-induced respiratory suppression. These include bradycardia, increased resistance to circulatory flow through gill capillaries, and erythrocyte swelling, resulting in their accumulation within the gill capillaries.

Etomidate and Metomidate Etomidate and metomidate provide a more rapid induction and recovery than MS-222. In sandbar sharks (Carcharhinus plumbeus), 10 mg of either drug-induced stage II anesthesia in approximately 2 to 4 minutes. This stage was characterized by an absence of response to positional changes, decreased respiratory rate to approximately normal, total loss of equilibrium, no righting response, decreased muscle tone, some response to strong tactile and vibrational stimuli, and adequate restraint for external sampling (e.g., gill biopsy). Increasing the dose to 20 mg reduced induction time to less than or equal to 1 minute, but anesthetic depth was more difficult to control. Although etomidate is considerably more potent than metomidate in freshwater teleosts, this difference was not observed in sandbar sharks. Recovery from stage II plane 2 took approximately 3 to 5 minutes for metomidate. Recovery from deeper planes was considerably prolonged (more than 1 hour), possibly because of decreased cardiac output (Stoskopf, 1986).

Halothane/Oxygen/Nitrous Oxide Dunn and Koester (1990) used halothane (1.5% for induction, then 0.5%

to 0.8% for maintenance) in nitrous oxide (100–200 ml/min) and oxygen (200–300 ml/min) for anesthesia of guitarfish (*Rhinobatas* sp.) and skate (*Raja* sp.). A precision vaporizer was used to add halothane to a mixture of nitrous oxide and oxygen, which was then introduced into the water through an aerator. This combination provides easy control of anesthetic depth, shorter recovery, and a very high survival rate. A major disadvantage is contamination of the working environment room with halothane and nitrous oxide.

Oxygen Oxygen narcosis can be used to immobilize some elasmobranch species for minor procedures. Oxygenated water is flushed across the gills by bubbling 100% oxygen in front of a power head directed into the mouth of the animal. Elevated dissolved oxygen levels (concentration dependent on elevation and temperature) usually have a sedative effect, likely a result from $\rm CO_2$ elevations due to respiratory depression. Prolonged exposure to elevated oxygen depresses ventilation and produces hypercapnia and potentially life-threatening acidemia (Spotte, 1992). Signs of oxygen sedation include depressed respiratory effort, behavioral changes, and loss of equilibrium. Since the oxygen is not provided under pressure, "gas bubble disease" does not occur.

Tricaine Methane Sulfonate (MS-222) Both sharks and batoids are anesthetized using 75 to 95 mg/L. MS-222 may be added slowly to evaluate effect. Buffering is always needed in freshwater systems and is especially important when inducing animals in open systems with high concentrations of MS-222 via hand pump. Gilbert and Kritzler (1960) demonstrated MS-222 (1 g/L) delivered through a hand pump sprayer anesthetized large sharks and rays. Buffering is also needed if you are repeatedly introducing MS-222 into small saltwater systems (i.e., serially anesthetizing many animals in the same water). The acidic solution should be buffered with sodium bicarbonate at a 2:1 (bicarb/MS-222) ratio or until the bicarbonate precipitates at the bottom of the container.

A direct linear relationship exists between MS-222 concentration and the time to muscular relaxation (Dunn and Koester, 1990). A wide variety of elasmobranch species achieve a surgical plane of anesthesia (i.e., stage 3) using MS-222 (75–95 mg/L), but speciesspecific responses are common (Dunn and Koester, 1990). Many sharks have been anesthetized using a low concentration (50 mg/L) as a "pre-anesthetic" dose followed by higher concentrations (less than or equal to 85 mg/L) for maintenance (Davis, personal communication). This "pre-anesthetic" concentration appears to reduce the excitement phase and lowers the overall maintenance level of MS-222.

Gilbert and Wood (1957) describe a field technique of bringing large lemon sharks (*Negaprion brevirostris*) up to the water surface with a hook and line and then applying a high concentration of MS-222 (1 g/L) with a

pump hand sprayer. Effects were noted within 15 seconds and the animals were anesthetized within 1 minute. It is recommended that the patient's head remain out of water and that only buffered MS-222 be applied to the gills.

MS-222 excretion in the piked dogfish (*Squalus acanthias*) is primarily through the gills and is a function of cardiac output (Maren, Embry, and Broder, 1968). Elimination of MS-222 into the water can result in a positive feedback of increasing anesthetic concentration if the heart slows, resulting in a possible overdose if the animals are not closely monitored.

INJECTABLE ANESTHESIA

Injectable anesthesia has several advantages over immersion. If performed carefully, it allows animals to be captured in large exhibits without the expense of excessive employee time and capital. Delivery is achieved by hand injection, pole syringe, Hawaiian sling, or remotely through an underwater dart gun (Harvey et al., 1988). Although several injectable drugs have been investigated in sharks, their use in batoids has not been reported.

Intravenous

Intravenous (IV) injection is the most reliable anesthetic delivery route, providing rapid induction and often a short duration of effect. The main disadvantage is that the animal must be appropriately restrained for drug delivery.

The most easily accessible blood vessel for IV injection, in both sharks and rays, is the vein that lies along the midline just ventral to the vertebral column. This vein is located by placing the needle just posterior to the trailing edge of the first or second anal fins. The needle is directed anteriorly an angle of 30 to 90°, relative to the body, and inserted approximately 4 cm for a 10-kg shark to penetrate the vein (Figure 15.1). This technique is used for both catheterization and drug administration (Stoskopf, Smith, and Klay, 1984).

Catheterization of the ventral coccygeal vein through a Tuohy needle permits medications to be given in a direct, consistent manner over a long period of time. In large sharks, needles may become plugged during penetration of the cartilage wall protecting the vessel. A spinal needle (with a removable stylet protecting the needle aperture) is used for most sampling or therapies in these larger animals. Intravenous injections can also be given in the lateral portal vessel, the dorsal lymph vessel, and even the heart by direct cardiac puncture (Tyler and Hawkins, 1981).

Walker (1972) calculated a circulation time of 1 to 2 minutes for indigo cyanine green injected in the caudal tail vein of nurse sharks (*Ginglymostoma cirratum*). Slow circulation may delay the onset of effect of an IV drug (e.g., propofol).

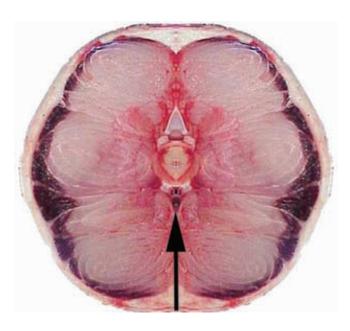


Figure 15.1. Cross section of the tail of a sandbar shark (Carcharhinus plumbeus) demonstrating the more vascular or "red" muscle in comparison with the "white" muscle. The arrow indicates the ventral entry of a needle to sample the caudal vein.

Intraperitoneal

Intraperitoneal (IP) (into the body cavity) injection requires drugs to pass through the serosal membranes of the coelomic cavity organs, making anesthetic induction time erratic. Needle insertion at an acute angle directed anteriorly to the pelvic girdle on the right side of the abdominal wall minimizes the possibility of puncturing any internal organs.

Intramuscular

Intramuscular (IM) injections are made either by hand to slow swimming sharks, pole syringe or other remote-injection devices (e.g., Hawaiian sling). Although very unlikely in a captive animal, an agitated shark can theoretically turn and attack the person administering the drug. Regardless of delivery, IM injection time is minimal, allowing reduced handling times.

Many sharks have both red and white muscle (Figure 15.1). The bulk of shark muscle tissue is white and has a relatively poor blood supply in comparison with that of red muscle. Injection into different muscles theoretically affects drug absorption. The variability in response to IM drugs within a species may result from this anatomical variation in blood supply.

The recommended site for IM injection is the dorsal saddle. This area surrounds the first dorsal fin and extends laterally to just above the lateral line, from the posterior gill slit caudal to a point halfway between the first and second dorsal fins (Stoskopf, Smith, and Klay, 1984). The protective denticles and epidermis requires the use of a heavy needle (16 to 18 gauge) to penetrate the tough integument. In addition, shark skin does not

have a great degree of contractibility and muscle is at a positive resting potential. These anatomical features may combine to allow drug leakage at the injection site. To minimize this, it is recommended that the needle be angled either anteriorly or posteriorly, depositing the drug away from the injection site. The author also leaves remotely injected darts in the animal until it has become sedated, thus preventing drug leakage.

Skeletomuscular movement helps blood and lymph circulate (Gruber and Keyes, 1981) and has a direct impact on IM drugs, which may not be adequately circulated in sedentary animals. Anesthetic induction time may be erratic or delayed, and injection of large volumes of drugs may form a sterile abscess in the musculature (Tyler and Hawkins, 1981).

Injectable Anesthetics

Alfaxalone-alfadolone Alfaxalone-alfadolone can be injected IM using a dart gun. Its use has been described in the piked dogfish (1.5 mL/kg), the brown ray (*Raja miraletus*) (0.2–0.3 ml/kg), the skate (*Dipturus batis*) (0.2 ml/kg), the black tip shark (*Carcharhinus limbatus*) (0.4 ml/kg), and the spotted eagle ray (*Aetobatus narinari*) (0.3 ml/kg) (Harvey et al., 1988). The anesthetic response was highly variable, from minimal effect in the eagle ray to immobilization in the dogfish.

Azaperone Azaperone reduces response to environmental stimuli without motor impairment or sedation. Preliminary studies in piked dogfish (Squalus acanthias) showed that the most efficacious application of azaperone is directly over the gills rather than by injection. No effect was noted when animals were injected with the drug IM. However, an effect was observed when the drug (4 mg/kg) was deposited on the gill filaments and the animal held out of water for several seconds (Latas, 1987). At 4 hours drugged animals, compared with control animals, showed no flight response. Blood glucose levels were unaffected. Tranquilized animals were more likely to feed compared with control animals, which exhibited several days of anorexia after blood collection. They were capable of negotiating tank walls and returned to normal behavior within 24 hours. The advantages of using azaperone include uninterrupted swimming patterns, normal gill ventilation, and normal cardiovascular function. Azaperone may be useful for animals that are prone to panic, aggression, and selfinduced trauma (Latas, 1987).

Carfentanil Citrate Carfentanil citrate (0.25 mg/kg) failed to achieve any effect in a nurse shark (*Gingly-mostoma cirratum*) and a lemon shark (*Negaprion brevi-rostris*). No effect was observed even when administered at massive doses (Stoskopf, 1986, 1993).

Detomidine Hydrochloride Two trials by this author using relatively high amounts of detomidine (115 μ g/kg IM)/ketamine (4.5 mg/kg IM) in a single bull shark

(Carcharhinus leucas) showed little effect. Atipamezole is given in equal volumes to the detomidine (5 times the µg dose) for reversal. In sharks, it is recommended that a full reversal dose be administered both IV and IM to smooth recovery. In the author's experience, all IV reversals have resulted in quick but often erratic recoveries. Smooth recoveries are imported to prevent damage to the sensory organs from disorientation and thrashing.

Ethanol Medium to large sharks (bull shark, *Carcharhinus leucas*; Dusky shark, *Charcharhinus oscurus*; tiger shark, *Galeocerdo cuvier*) have been reported to be affected by IP injection of 47.5% ethanol (less than or equal to 113 kg 1.1 ml/kg; larger animals 0.55 ml/kg) (Sudak, 1966). Animals were visually unaffected at 50 minutes, but could be in dorsal recumbency for up to 1 hour. It is not clear whether this was a state of tonic immobility. Animals showed effects at 3 to 4 hours, but appeared normal at 24 hours. The types of effects were not stated. A dusky shark (*Carcharhinus obscurus*) died during anesthesia, but it may have struck a pylon because of its decreased ability to maneuver.

Ketamine Hydrochloride Ketamine hydrochloride is an analgesic and cataleptic cycloheximide. Ketamine provides good peripheral analgesia (pain relief) in mammals through suppression of dorsal horn cell activity in the spinal cord, but provides little visceral analgesia. Seizure-like muscle spasms resulting from spinal reflex firing are occasionally noted in elasmobranchs (Stoskopf, 1993). For these reasons it has only been used in combination with other anesthetics.

Medetomidine Medetomidine has been used in combination with ketamine in several shark species, including sandtiger shark (*Carcharius taurus*), blacknose shark (*Carcharinus acronotus*), sandbar shark (*Charcharhinus plumbeus*), and nurse shark (*Ginglymosoma cirratum*) to ameliorate muscle spasms that can occur with ketamine alone (Snyder et al., 1998). See medetomidine/ketamine combination for effects. Atipemazole is used as the reversal agent.

Propofol Mitchell et al. (2001) administered propofol (2.5 mg/kg IV) over 30 seconds to spotted bamboo sharks (*Chiloscyllium plagiosum*), achieving a surgical anesthetic level by 5 minutes. Righting response returned within 60 and 75 minutes in four and two of the sharks, respectively. Respiration and heart rates remained stable throughout the anesthetic period.

Sodium Pentobarbital Sodium pentobarbital (10 mg/kg rapid IV via caudal vein) produced satisfactory general surgical anesthesia in nurse sharks (*Ginglymosoma cirratum*) (Walker, 1972). Slow injection resulted in an erratic response. Intraperitoneal absorption was slow and response was variable, whereas IM injection resulted in

only slightly improved response. Serum half-life was approximately 15 seconds with a second half-life of several days, owing to an inability of the animals to excrete the drug through their gills or kidneys. An anesthetic IV dose (10 mg/kg) resulted in loss of ventilatory movements (gilling) within 1 minute. Gilling returned after 10 minutes and a weak righting response was observed at 3 hours. A higher IV dose (20 mg/kg) resulted in a rapid loss of gilling that did not return by 3 hours. A weak righting response was only observed after 5 hours. A high IV dose (60 mg/kg) resulted in death. Larger, more active sharks require smaller doses per kilogram than smaller, sedentary specimens. For example, sandbar and bull sharks (6 mg/kg IV) responded similarly to the nurse shark (10 mg/kg IV) (Walker, 1972).

Tiletamine/Zolazepam Tiletamine/zolazepam (12 mg/kg) administered to a lemon shark (*Negaprion brevirostris*) and a sand tiger (*Carcharias taurus*) shark produced irritability, rapid swimming and unrestrained biting (Stoskopf, 1986, 1993).

Xylazine Xylazine in boney fish (teleosts) is a convulsant and causes major changes in the electrocardiogram (Oswald, 1978). Used in combination with ketamine (12 mg/kg), xylazine (6 mg/kg) in sandtiger shark (*Carcharius taurus*), lemon shark (*Negaprion brevirostris*), sandbar shark (*Charcharhinus plumbeus*), and nurse shark (*Ginglymosoma cirratum*) variably ameliorates the muscle spasms that can possibly occur with ketamine alone (Stoskopf, 1993). Yohimbine hydrochloride administered IV to a nurse shark immobilized with xylazine/ketamine caused arousal (Stoskopf, 1986).

Injectable Anesthetic Combinations

Several drug combinations have been or are currently being investigated for immobilization or anesthesia of elasmobranchs. Stoskopf (1986) showed xylazine (6 mg/kg)/ketamine (12 mg/kg) satisfactorily immobilized (between stage I and III) sandtiger (*Carcharius taurus*) (n = 4), lemon (*Negaprion brevirostris*) (n = 4), sandbar (*Charcharhinus plumbeus*) (n = 9), and nurse sharks (*Ginglymosoma cirratum*) (n = 5). Andrews and Jones (1990) also found xylazine (7.5 mg/kg)/ketamine (16.5 mg/kg) produced light anesthesia adequate for the safe transport of adult sandbar sharks (*Charcharhinus plumbeus*).

Medetomidine (90–100 µg/kg IM)/ketamine (4–5 mg/kg IM) is being investigated by the author. The drug combination usually takes around 20 minutes but can be erratic. Effects vary from complete anesthesia within 5 minutes to animals showing partial signs, but no recumbency despite additional dosing. There also appears to be a great variation between species in their responses to similar dosages under the same conditions. Importantly, all animals have shown appropriate orientation throughout all full and partial inductions.

Potential Anesthetic Drugs

Eugenol (Clove Oil) The over-the-counter drug eugenol has been used in Teleosts, but its use in elasmobranchs (Sladky et al., 2001) has not been described.

Diazepam Diazepam in sandbar (1.2–1.6 mg/kg PO) and sandtiger (0.1 mg/kg IM) sharks provided satisfactory sedation, but more research is indicated to further define dosages (Mylniczenk; McEwan, personal communication).

Nonspecific Reversal Drugs

Doxapram Hydrochloride Doxapram hydrochloride has been noted to produce dramatic arousal in anesthetized elasmobranchs (Stoskopf, 1986). However, doxapram causes stimulation and should be used with caution because animals can become extremely excited and dangerous.

SUPPORTIVE CARE AND EMERGENCY DRUGS

Anesthetized or immobilized sharks and rays should be carefully monitored. Animals exhibiting progressive bradypnea or bradycardia should be placed in fresh seawater or seawater with lower anesthetic concentrations. If anesthetized with an injectable anesthetic, the reversal should be given. Unresponsive animals are administered fluids, doxapram, and forced ventilation.

Emergency fluid therapy should take into account the animal's osmotic balance, as well as urea, NaCl, and trimethylamine oxide which are the major osmoregulatory plasma components in elasmobranchs (Olson, 1999). A balanced salt solution is made by adding 8 g/L NaCl and 21.02 g/L urea to phenol red-free Hank's balanced salt solution (Andrews and Jones, 1990). This can be administered through a catheter placed in the caudal vein or intraceolomically. No dose rates of administration have been established but the author uses shock rates used for other animals. Elasmobranchs appear to respond to oral freshwater administration at 1% to 3% body weight in less severe situations.

As described, elasmobranchs may respond to doxapram with explosive excitement. Other traditional mammalian emergency drugs (e.g., corticosteroids) are given in the case of physiological collapse.

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16 Amphibians Mark Stetter

INTRODUCTION

Amphibians are native to all continents, except Antarctica, and are routinely maintained in captive situations as pets, in laboratories and zoological settings. They reside in a wide variety of habitats including aquatic, semi-aquatic, and terrestrial. Amphibians are found from the equatorial rainforest to Canada, where they may remain frozen through the winter. There are more than 4,000 species, including frogs, toads, salamanders, newts, and caecilians (Crawshaw, 2003). There is a growing concern about worldwide amphibian declines and its implications for global ecosystem health.

Veterinarians are most likely to be involved with captive anurans (frogs and toads) or urodeles (salamanders and newts). It is not uncommon for amphibians to require sedation or anesthesia for diagnostics, surgery, or research.

ANATOMY AND PHYSIOLOGY

Amphibians have several unique and clinically relevant anatomical characteristics. The first is they go through metamorphosis and change from strictly aquatic larval (i.e., tadpoles) to terrestrial adults. These metamorphoses include dramatic anatomical changes; growth of legs, loss of gills, and formation of lungs. As a completely aquatic tadpole with gills, they have a very similar respiration to fish. As adults with lungs, they can leave their aquatic environment and respire out of water. For these reasons it is impossible to drown a tadpole, but an anesthetized toad immersed in water can aspirate through its nose and drown. The unique semipermeable amphibian skin allows anesthetic drugs and oxygen to cross. This is very useful for application of anesthetic drugs topically with systemic effects. It also allows animals to respire and maintain appropriate blood oxygen levels without pulmonary respiration (Stetter, 2001; Wright and Whitaker 2001; Crawshaw, 2003).

GENERAL ANESTHETIC CONSIDERATIONS

Their aquatic nature and skin permeability make amphibian anesthesia very similar to fish anesthesia in

methodology and drugs used (Stetter, 2001). The anesthetic compounds are most commonly delivered in water and absorbed across the animal's gills or skin. Inhalant anesthetic agents are delivered into a chamber containing the animal or bubbled into the water, but this is often a time-consuming process. Although there are some published dosages of injectable anesthetic agents, in the author's experience these are often unreliable, have a very low margin of safety, may be associated with a prolonged recovery, and dosages are very species specific (Stetter, 2001; Wright and Whitaker, 2001; Crawshaw, 2003).

Even entirely aquatic amphibians can be kept out of water for extensive periods of time. In all cases the skin is kept moist throughout the procedure to prevent damage and dehydration and ensure dermal respiration is maintained (Wright and Whitaker, 2001). When working with entirely aquatic species (e.g., African clawed frog, Xenopus laevis), tank water from the animal's environment is ideally used. This reduces exposure to abrupt environmental changes (i.e., temperature, pH, etc.). All water used for anesthesia is tested using standard reagent test kits to ensure there are no deleterious elevated variables, such as ammonia (Wright and Whitaker, 2001). Toxin-free (dechlorinated) water within the animal's preferred body temperature range (usually 15–23°C, 59–73°F) is used (Wright and Whitaker, 2001). Bottled water at room temperature is often a convenient standard for use.

Whatever container is used for an anesthetic chamber, it must be thoroughly cleaned and rinsed. Because amphibians absorb chemicals across their skin, cleaning solutions or other chemicals left in a container can be toxic. In addition, amphibians secrete toxins from their skin and it is important to rinse containers well between patients. Sealable plastic bags are efficient containers for anesthetic bath induction chambers and can be discarded when the administration is complete (Figure 16.1). Other potential induction chambers include small plastic containers with lids (Figure 16.2) or small fish aquariums. Many amphibians exhibit an excitement phase during induction making it important to have an enclosed container to prevent the patient leaping out

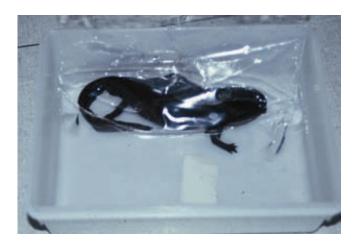


Figure 16.1. Salamander being anesthetized in a water-filled sealable plastic bag. Anesthetic water solution is placed within the bag and the closed container prevents animal escape during any form of an excitement phase. Holes can also be cut in the corners of the bag after induction so that water can drain out and the animal can be moved or positioned (e.g., for a radiograph) with minimal handling.

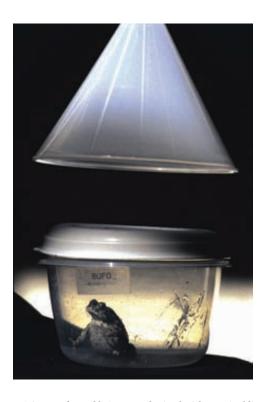


Figure 16.2. Bufo toad being anesthetized with a topical liquid isoflurane solution in a closed plastic container. A scavenger system has been attached to the funnel, which is inverted above the container to remove any isoflurane vapors.

(Stetter, 2001; Wright and Whitaker, 2001; Crawshaw, 2003). When a water bath is being used for anesthetic application, there should be an interface with the air at the surface (i.e., do not fill the container completely to the lid). Animals with lungs are removed from the water after induction to ensure they do not aspirate. Although the risk is low, it is prudent to wear latex gloves and wash

hands whenever working with a potentially toxic amphibian species (e.g., toads of the *Bufo* genus) (Stetter, 2001; Wright and Whitaker, 2001; Crawshaw, 2003). The talc commonly found on latex gloves is rinsed off and the gloves moistened to prevent irritation to the amphibian's skin.

Amphibians do not require fasting prior to anesthesia. Their larynx remains tightly closed even under general anesthesia and the chance of aspiration is very low (Wright and Whitaker, 2001). However, if the amphibian's diet is large prey items (e.g., rodents) it is not fed 24 to 48 hours before anesthesia. This assists visualization during coelomic surgery and ensures there is no gastrointestinal disruption (ileus) associated with anesthesia and decreased metabolic processes.

MONITORING

The skin under the mandible and along the ventral neck is the gular region; movement in this area is a primary means of respiration. As a patient becomes anesthetized, gular respirations decrease and there is a diminished withdrawal reflex (Stetter, 2001; Wright and Whitaker, 2001; Crawshaw, 2003). Light anesthesia is associated with loss of righting reflex and an absence of abdominal respirations (Figure 16.3). Surgical anesthesia is indicated by a loss of withdrawal reflex and cessation of gular respiration (Stetter, 2001; Wright and Whitaker, 2001; Crawshaw, 2003). Since anesthetic induction in amphibians is often a hands-off technique, where the patient is in a small sealed plastic bag or container, the author uses the righting reflex as a primary indicator to determine the stage of anesthesia. When the patient has ceased movement and appears to be anesthetized, the entire chamber is inverted to see if the amphibian has lost its righting reflex. For procedures requiring light anesthesia (e.g., blood sampling, radiographs, physical examinations, etc.) the patient is removed from the container and quickly rinsed with anesthetic-free water before the procedure begins. If surgical anesthesia is required, an aggressive toe pinch of the rear leg will help determine if the patient can be removed from the chamber.

Anesthetized amphibians usually become apneic; abdominal and gular respirations cease. This can be very disconcerting for the anesthetist who relies on respiratory rate for assessing anesthesia. The dermis is kept moist since dermal respiration will now be the primary method of oxygenation. Cutaneous respiration will be adequate to prevent clinical hypoxemia in anesthetized amphibians (Stetter, 2001; Wright and Whitaker, 2001; Crawshaw, 2003). For long surgical procedures the patient is placed in a shallow water bath that has oxygen bubbled into it (Figure 16.4). Amphibians rarely need to be intubated. With larger animals or if oxygenation is a concern, a soft rubber tube can be used for intubation. The trachea is very short and the tube is placed just past



Figure 16.3. Anesthetized bufo toad in dorsal recumbency. General anesthesia has been confirmed by a loss of righting reflex and cessation of gular respirations [(A) indicates the gular region of the neck]. The heart beat can be directly visualized just between the forelegs (B).



Figure 16.4. Anesthetized bufo toad is in an anesthetic water solution into which oxygen is bubbled (arrow). ECG leads have been placed to monitor the heart rate and a sterile dressing has been placed over the ventrum in preparation for surgical exploration.

the larynx (Stetter, 2001). Amphibian lungs are composed of thin-walled membranes and manual ventilation is done gently.

Heart rate is a useful tool for anesthetic monitoring (Wright and Whitaker, 2001; Crawshaw, 2003). In most anesthetized patients in dorsal recumbency, the heart is seen contracting on the midline just caudal to the animal's shoulders. Direct visualization, ultrasonography, or a Doppler monitor are used to measure heart rate



Figure 16.5. Anesthetized frog in an anesthetic water bath. An ultrasound probe is being used to monitor heart rate in the anesthetized patient.

(Stetter, 2001; Wright and Whitaker, 2001; Crawshaw, 2003) (Figure 16.5). Although normal heart rates for species are not extensively published, a significant decrease in heart rate is of concern and indicate excessive anesthetic depth. Pulse oximetry has not been validated in amphibians, but may show trends in hemoglobin saturation for long procedures. Intermittently monitoring withdrawal reflex will determine if the patient is transitioning from surgical to light anesthesia. A patient that regains its withdrawal reflex, or gular respirations, requires supplementation if a surgical plane of anesthesia is still required. For supplementation, a 50% concentration of the original solution is applied topically via syringe or partial water bath. When the animal reaches an adequate level of anesthesia the application is discontinued.

ANESTHETIC DRUGS

Tricaine Methanesulfonate (MS-222 or Finquel)

This is the most commonly used anesthetic for amphibians (Downes, 1995; Stetter, 2001; Wright and Whitaker, 2001; Cooper, 2003; Crawshaw, 2003). It is effective in all species, with all developmental stages of amphibians, and it has a wide margin of safety. It is also the only FDA approved anesthetic in fish and can be acquired through aquaculture distributors (Wright and Whitaker, 2001).

Tricaine methanesulfonate is a white powder that easily dissolves in water. As it dissolves the water becomes very acidic, especially at higher concentrations and with waters that have a low buffering capacity (Downes, 1995; Stetter, 2001; Wright and Whitaker, 2001; Crawshaw, 2003). This acidic solution is not only irritating to the patient, but is also less effective as an anesthetic at these low pH levels. It is, therefore, important to buffer the solution and keep the pH at 7.0 to 7.5 (Downes, 1995; Stetter, 2001; Wright and Whitaker,

2001; Crawshaw, 2003). This is easily accomplished by adding sodium bicarbonate to the mixture. Common baking soda (powdered sodium bicarbonate) is added to the solution until saturation (powder no longer dissolves) is achieved. Because the patient is being induced in an anesthetic water bath, body weight and anesthetic dosages (mg/kg) are not relevant. The anesthetic concentration in the water bath is determined by the level of sedation or anesthesia required along with relative life stage of the amphibian (tadpole vs. adult), as well as the type of amphibian (Downes, 1995; Stetter, 2001; Wright and Whitaker, 2001; Crawshaw, 2003). In general, much lower concentrations are required for younger larval stages and for the more aquatic frogs compared with the terrestrial toads. Concentrations of 0.25 to 0.5 g/L (0.05%) are used for amphibian stages where gills are present (Stetter, 2001; Wright and Whitaker, 2001; Crawshaw, 2003). Levels of 1 to 2 g/L are commonly used for frogs and salamanders (Cooper, 2003; Crawshaw, 2003). Concentrations in the 2 to 3 g/L range are used for the thicker skinned terrestrial toad species (Stetter, 2001; Wright and Whitaker, 2001; Crawshaw, 2003).

Once water volume is known the exact amount of tricaine methanesulfonate is weighed out, dissolved in the water, and the buffer is added to saturation. This solution is then labeled with the drug content and concentration. This solution is not stable over long periods of time and is discarded after each use. The anesthetic solution is now placed in a sealed plastic bag or food container. The level of the water is enough to cover approximately half of the patient's body. Although induction times are variable, the effects are usually noted within 15 minutes, with full effect often taking 30 minutes. For animals with gills induction rates are more rapid.

ISOFLURANE

Isoflurane is a safe and effective anesthetic agent in amphibians and may be familiar and valuable to the practitioner who does not keep MS-222 in stock (Stetter, 2001). Isoflurane is delivered in the traditional vaporized form via a chamber or by bubbling vaporized isoflurane and oxygen from an anesthetic system into a water bath (Stetter, 2001; Wright and Whitaker, 2001; Crawshaw, 2003) (Figure 16.6). In both cases a sealed container is used to minimize human exposure and increase isoflurane concentrations in the air chamber. Although these methods are effective, they are associated with slow induction times and rapid recoveries once the patient is removed from the chamber. Other effective and longer-lasting methods of isoflurane anesthesia include application of liquid isoflurane to either the skin or a water bath (Stetter, 2001). For the water bath, a syringe is used to spray the liquid isoflurane directly into the water through a 25-g needle. The



Figure 16.6. Vaporized isoflurane is being bubbled into a water bath to anesthetize an axolotl. This technique is effective but associated with slow induction times. A closed container can help reduce induction times and minimize exposure to isoflurane gas.

needle tip is placed below the surface of the water and the isoflurane liquid is injected and mixed into the water bath. A concentration of 2 to 3 ml/L is most commonly used (Stetter, 2001; Crawshaw, 2003).

When applying the liquid isoflurane directly to the dermis, a carrier solution is created to increase dermal contact time prior to the isoflurane being vaporized. A mixture is created using 3 mL of liquid isoflurane, 1.5 mL of water, and 3.5 mL of K-Y Jelly (Stetter, 2001). These three items are placed into a 10-mL empty serum vial and vigorously shaken until a uniform gel is established. This isoflurane gel can now be administered to the patient's dorsum at dosages of 0.025 to 0.035 ml/g body weight (Stetter, 2001). Lower dosages are used for more aquatic species and higher dosages for thicker skinned terrestrial species (e.g., toads). After the isoflurane gel is mixed in the vial the indicated volume is withdrawn through a syringe and a 16-g needle and the gel deposited on the patient's dorsum. Once applied, the patient is placed in a small sealed container until induction is complete. After induction, saline-soaked gauze is used to remove the anesthetic gel preparation from the patient's skin, or the patient is rinsed in toxin-free water. Patients anesthetized with topical isoflurane gel remain under anesthesia for 45 to 80 minutes. Shorter anesthetic times with a more rapid recovery are seen with the liquid isoflurane in water method (Stetter, 2001).

MISCELLANEOUS TOPICAL ANESTHETIC DRUGS

A wide variety of drugs traditionally used for local analgesia in mammals have been successfully used in amphibians. A topical xylocaine spray (10% solution) has been successfully used in large frog aquaculture systems (Garcia Aguilar, Palcios Martinez, and Ross, 1999). The commercially available product, Orajel,

containing 10% to 20% benzocaine has been successfully utilized in salamanders and anurans (Brown, Tyler, and Mousseau, 2004).

Eugenol (clove oil) has recently become popular as an immersion anesthetic agent in fish. Early trials with frogs, using a concentration of 0.3 to 0.5 ml/L indicate some potential value as an anesthetic (Lafortune, Mitchell, and Smith, 2000; Crawshaw, 2003).

INJECTABLE ANESTHETIC DRUGS

A variety of injectable anesthetic agents, including ketamine, tiletamine/zolazepam, tricaine, and various barbiturates have been used in amphibians. In general these agents are less reliable than the inhalant and topical anesthetic agents. They are also associated with large species variability in effect and have been known to produce significantly higher mortality rates.

RECOVERY

Recovery from anesthesia is relatively prolonged compared to other animals. In general, vaporized inhalants such as isoflurane in a chamber provide rapid recovery rates versus topical application methods (Stetter, 2001). As the animal begins its recovery, the

withdrawal reflex and gular respirations are the first to return followed by the righting reflex (Stetter, 2001; Wright and Whitaker 2001).

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17

Crocodilian Capture and Restraint

Kent A. Vliet

INTRODUCTION

Anesthesia and chemical immobilization of crocodilians almost always requires some form of confinement and physical restraint for drug administration and to prevent them from seeking refuge in their aquatic environment. Anesthesia and immobilization are discussed in Chapter 18; the following is a description of capture and restraint techniques that minimize the potential for injury to handlers and animals.

Crocodilians are dangerous; they are capable of injuring, scarring, maiming, and even killing handlers. This is not to imply they are bad, loathsome, or evil. It is simply the result of being large, tremendously powerful, predatory, agile, and adaptable. No one can safely work with these animals until this is fully comprehended. Further, you must remind yourself of this every time you work with them; complacency is our greatest threat.

There are many ways to safely capture and restrain even very large crocodilians. There are a greater number of incorrect ways. Each capture is different and always has the potential to go wrong. Many variables must be taken into account in successfully capturing and restraining a crocodilian.

Ultimately, no amount of detail in this chapter, training, or experience will guarantee no harm to those working with these animals. If you can not personally accept this liability, you should neither attempt any of the techniques discussed in this chapter, nor work with crocodilians. Accepting this liability is part of the commitment necessary to work with these magnificent animals.

For larger captive crocodilians the trend is to reduce contact with the keeper staff by providing shift enclosures and training the animals to use them. This is much preferred over physically capturing and restraining an animal. Although the former (shifting) is strongly encouraged, the latter (capture and restraint) forms the body of this chapter.

Few publications describe techniques for the safe capture, restraint, and handling of captive crocodilians.

Most descriptions are of free-living species: for example, the American alligator (Alligator mississippiensis) (Chabreck, 1963; Jones, 1965; Joanen and Perry, 1972; Murphy and Fendly, 1974; Forster, 1991; Jones and Hayes-Odum, 1994; Wilkinson, 1994); the American crocodile (Crocodylus acutus) (Mazzotti and Brandt, 1988); the Nile crocodile (C. niloticus) (Pooley, 1984; Hutton, Loveridge, and Blake, 1987; Kofron, 1989); and the saltwater crocodile (*C. porosus*) (Webb and Messel, 1977; Walsh, 1987). Although useful insights and methods are gleaned from these papers, most describe traps that are of little practical application in the captive environment. A detailed list of equipment and techniques used in alligator research is found in McDaniel and Hord (1990). Fowler (1978) makes brief mention of restraint of smaller captive crocodilians. Almandarz (1986) describes physical restraint techniques of reptiles, including crocodilians. The most comprehensive reference is that of Wise (1994). This article contains many pertinent and useful insights that serve as a valuable reference for anyone interested in developing the skills necessary to safely work with these animals. The following discussion builds on and expands the contributions of these

This chapter does not detail all of the possible techniques for capture and restraint. The author has included those he is experienced with, accustomed to, and believes provide enhanced safety. The author has had the opportunity to capture all 23 crocodilian species during several thousand captures over 20 years, in both captive and free-living situations. Techniques evolve, and new and better practices come into use. Others may have different, and even better, methods than those presented here.

CAPTURE EQUIPMENT

Crocodilians frequently damage and destroy capture equipment. Consequently, restraint is either an

expensive exercise or one develops sets of equipment that are easy and inexpensive to manufacture. The latter allows an adequate supply of equipment to always be available. The standard equipment the author and staff of the St. Augustine Alligator Farm and Zoological Park use for crocodilian capture and handling is described in the following.

Ropes

Capture Ropes Ropes are essential for most captures; they are used to gain a hold on and restrain, and for the safe release of animals. Several ropes are always available for any capture. The size used depends on the crocodilian to be captured. Smaller specimens require smaller diameter ropes, while larger animals necessitate thicker and stronger ropes. Too small ropes may cinch too tightly on the animal or burn into a keeper's hands during a struggle. Ropes of too great a diameter will not close tightly enough over the neck or jaws, allowing the animal to work itself free.

For adult animal captures, the author uses either 1.3-cm (1/2-in.) or 1.6-cm (5/8-in.) ropes. They can be sisal (hemp), nylon, cotton, or a mixture. Ropes have different tensile strengths; it must be adequate for the size and mass of the animal to prevent breakage and animal escape. Nylon ropes are generally the strongest. Cotton and sisal work well for many purposes, but rot if not allowed to dry after use. This leads to problems during captures of large animals; the rope may separate under tension, allowing the animal to go free and the keepers to fall back and possibly injure one another. Woven or braided ropes are less likely to kink or fail than twisted ropes. Many ropes float on the water surface preventing their placement under the head of a submerged crocodilian. Consequently, ropes are assessed before purchase and use for their ability to sink when soaked. The best ropes the author has used are those designed for arborists. They are soft and pliable yet strong, and they do not tend to "burn" hands when jerked by a crocodilian. However, they are also expensive.

Rope length depends on the intended use. Excessive length makes it difficult to gather and control during hectic moments in captures. The author frequently lassos crocodilians from a distance. For large crocodilians, several people are needed to pull a roped animal from the water or to a position where it can be safely secured. For these purposes, the author uses 8- to 9-m (25 to 30 ft) ropes.

Restraint Ropes Smaller-diameter and shorter ropes are ideal for restraint. Ropes of 0.6 (1/4-in.) or 1 cm (3/8-in.) diameter are used to tie the legs off of the ground to prevent movement, or tie down an animal to a ladder or platform.

Jaw Ropes Jaw ropes are used to tie the jaws shut or remove the tape off of an animal's jaws as it is being

released. These are generally small diameter, 0.3- (1/8-) to 0.5-cm (3/16-in.), and shorter, 3- (10) to 3.7-m (12-ft) ropes. Cotton clothes line works well for this purpose.

Poles

Defensive The primary use of a defensive pole is for protection of the handler(s). They must be of sufficient diameter and heft to maintain a safe distance between the holder and crocodilian during capture. When charged or lunged at by an overly enthusiastic animal, block the animal's advance and move to the other side of the pole.

These poles serve many other purposes. Animals can be discouraged from advancing toward a handler by lightly laying the pole on the soft tissues of its nostrils, or against its earflap. Similarly, animals are encouraged to move out of the way, allowing access to a particular animal for capture. In addition, the pole is used after capture to manipulate and position the animal (e.g., move legs, lift jaws, force the jaws shut, etc.) without getting too close.

Defensive poles are generally wooden; if they are bitten by an animal they do not cause significant damage to the teeth. The author uses a heavy, large-diameter length of bamboo approximately 1.5 (5 ft) to 1.8 m (6 ft) in length.

Poles greatly increase safety while working in close proximity to crocodilians. However, care must be taken when using them with larger crocodilians. Poles can become dangerous to personnel if grabbed and held in the crocodilian's jaws. When the animal swings its head from side to side the pole may strike and injure a person. Care must also be taken when recovering a pole from a crocodilian.

Catch A variety of catch poles are used to grab and hold. They all include a long rod with a noose or snare at one end. For larger animals (greater than 2 m) poles are designed so the noose and rope attachment separates from the rod. Commercial catch poles are used when no other poles are available. They are sturdy and give very good control over the animal. However, even relatively small crocodilians (greater than 1.5 m) roll or spin violently enough during capture to twist and kink the cable snare, thereby destroying it. Further, during a struggle the metal rotating cuff adjacent to the snare will push into the animal's head and neck and cause injury. Frequent use of commercial catch poles is not recommended because of initial purchase cost, and the expense and time of repeated repair and maintenance.

Alternatively, it is easy, quick, and very inexpensive to make catch poles. There are three commonly used, simple designs. The preferred is a "break-away" rope noose secured to the end of a pole with electrical tape. Once the rope is placed over the head and neck of the animal, the pole is pulled free and removed from the capture area. Recommended poles for this design are



Figure 17.1. A home-made cable snare used for catching small to medium-sized crocodilians. The catch pole is made of PVC piping.

long (3 to 5 m), 3- to 4-cm (1 1/2-inch) diameter wooden rods or lightweight aluminum electrical conduit. Swimming pool net poles also can be used; they are lightweight, long, and extensible.

Schedule 40 PVC pipes can also be used to make other catch poles. Snares are made of twisted metal cable and affixed to the end (Figure 17.1). The snare is attached by a metal swivel coupled to an eyebolt through an end cap. The cap is glued onto the end of the PVC pole (Figure 17.1). An advantage of this design is that snares of different diameter, or that have become damaged during a capture, can be rapidly exchanged during a capture. A small wire is attached to the snare base to keep it open until in place on the animal. Surprisingly, jacketed cables with plastic coverings cause more skin damage than exposed metal cables.

The simplest homemade catch pole for animals less than or equal to 2 to 3 m (8–9 ft) consists of a nylon or cotton rope run through a length of 1.5 to 2 cm (1/2- to 3/4-in.) PVC pipe (Figure 17.2). The rope is secured through a hole drilled in the pipe wall close to the end, then run out of the pipe and back in again, to form the noose, and then down the length of the PVC. When the noose is placed around the animal, the rope extending from the back end of the pole is pulled tight and bent back against the pole for added friction. PVC pipes bend and fracture if they are used to lift animals. Once secured with the noose, the restrainer pulls back in line with the direction of the pipe to pull the animal for positioning and restraint.

Mouth A short version of the noose design works exceedingly well as a mouth pole for closing and securing the jaws of captured crocodilians prior to taping or tying. The noose is placed over the jaws and tightened.



Figure 17.2. A home-made rope snare used for catching small to medium-sized crocodiles. It can also be used as a jaw noose; the rope is placed around the upper and lower jaws and either twisted or the rope pulled at the distal end to tighten. The pole is made of PVC piping.

Once the jaws are shut, the pole is twisted several times to add more tension to the noose. A person then steps in to quickly secure the jaws.

Tape

Tape is essential after capture and during restraint; jaws can be safely secured and heavier tapes are used to immobilize legs to prevent movement. The most commonly used are silver duct and black PVC electrician's tape. Always have a sufficient amount on hand.

Cable Straps

Nylon cable straps (zip ties) are very useful for securing the jaws of some crocodilians (i.e., narrow-jawed species) even before one captures the animal. These come in various lengths and tensile strengths; the largest can resist a force of 100 kg.

Shelf Mat, Rubberized

Shelf mats are made of rubber-coated, woven fabric. They are used as non-skid shelf coverings and are readily purchased. The mats are cut into 5- to 10-cm (2- to 4-in.) wide strips to wrap around the snout or the entire head. They are used for this purpose because they do not slip in a wet environment. The crocodile jaws are held shut with a mouth pole or by hand, wrapped with the mat, and then taped over. The sponginess of the mat prevents the tape from binding too tightly. Also, the non-slip nature of this material prevents jaw tape from slipping forward and covering the nostrils during transport.

Eye Cloth

The eyes are covered before or after capture with a cloth, towel, burlap bag, or old T shirt. This has a calming effect on the animals and likely reduces stress during the

capture period. The blinded crocodilian is much less likely to avoid capture and struggle following capture. Additionally, if the animal does attempt to strike, it is undirected and less likely to injure. Eye cloths are safely and gently placed over the eyes using a hook.

The cloth is soaked before placement so it will more completely cover the eyes of the partially submerged crocodilian.

Eye clothes are secured with a couple of wraps of duct tape. Crocodilian eyes can be voluntarily withdrawn down into the skull, but some caution must be used when taping the eye cloth. Do not press the eyes too hard or apply too much pressure with the tape. If the eyes are to be covered for an extended period, gauze pads or a folded paper towel are placed over them before taping.

Hooks

Hooks are absolutely essential tools when working with crocodilians. They facilitate work around the animals by allowing placement of ropes, manipulation of legs, etc., without bringing human appendages within striking range. Several different hook types have been used by the author. Heavy snake hooks (e.g., python hooks) are sufficiently robust for positioning ropes around a crocodilian's head, lifting legs, lifting the jaws, etc. Hooks are also useful for removing and retrieving ropes during release.

The author also uses long, very lightweight fiberglass hooks designed for livestock showing (Figure 17.2). These break fairly easily, but are also inexpensive. They are not substantial enough to manipulate an animal, but are excellent for rope noose placement and positioning. When capturing a submerged crocodilian, it is often possible to carefully position a rope noose over and around the head with these hooks without disturbing the animal and causing it to move.

Restraint and Transport Devices

Once captured and the jaws secured, there are many ways to confine or restrain a crocodilian (e.g., bags, buckets, ice chests, shipping crates, ladders, platforms, and cargo nets or marine mammal slings). The restraint technique and equipment selected depends on: (1) animal size; (2) duration of confinement; and (3) distance to be transported. A more detailed discussion of these devices is given in the following.

Knives and Other Tools

Cutting implements are always available during a capture. Knives are used to cut tape, frayed rope, etc. Wire cutters are used to cut through cable straps when used on the snouts of some specimens.

Trauma Kit

If the capture techniques described in this chapter are followed, the risks to personnel are minimized. However, the capture team should always be prepared

for someone being injured during restraint. This includes having a well-stocked trauma kit on hand to provide immediate aid.

TO CATCH A CROCODILIAN

As described, crocodilians can be massive, powerful, and often react violently to physical restraint. During capture, safety of personnel is paramount, followed closely by the welfare of the animals. The techniques favored by this author restrain the animals completely to limit the possibility of self-injury to the animal as well as personnel injury. The essential components of successful capture are planning, communication, caution, and knowledge of the animals.

Planning and Preparation

Capture and restraint of small specimens is usually routine and does not necessitate much planning or preparation. This is absolutely not the case when attempting to capture and restrain a larger specimen (i.e., greater than 2 m, 6 ft in total length). Preparation includes careful planning, discussion, and oversight. One person (the team or crew leader) is designated to be in charge, and he or she tells everyone else what to do, where to be, etc. Each person's role or roles is discussed and clearly understood before the operation commences.

However, many plans are quickly rendered moot if the capture subject is uncooperative. Each capture experience is different; it is not possible to foresee all of the variables likely to be encountered. Flexibility and strategy, the ability to change capture plans in mid-course while still maintaining a safe working environment, are essential. As handlers become more experienced with captures they develop a greater repertoire of techniques to apply to specific situations.

Communication is essential before, during, and after a capture to ensure the safety of the staff and the animal. Each team member must listen for, and continue to receive instructions from, the team leader throughout the procedure. The team leader must also continually look out for crew safety, make sure staff members are in their proper positions and performing their assigned roles, everyone is outside of the strike zone of the animal, and escape routes are kept clear at all times.

Environmental Assessment

The first stage of preparation is assessment of the capture environment. If the animal is in a simple off-exhibit enclosure this may be fairly straightforward. However, an animal on display in a complex habitat full of obstacles and possibly with other enclosure mates requires more forethought. It is important to answer several questions when assessing the capture environment.

Where Are the Escape Routes This is perhaps the most important question. More than one route is preferred, but often not available. All team members must be aware of these routes, and they are left clear at all times during the capture.

What Is Physically Possible? The geography of an enclosure determines access and the capture technique used. For example, low overhanging vegetation, large amounts of vegetation, and logs or rocks in a pool make it difficult to get a rope on an animal.

Is the Animal Trained to Shift? Many institutions provide off-exhibit shift areas, similar to those used for mammalian carnivores or large hoofed stock. Crocodilians can be rapidly trained with food to use these shifts, and even to move into transport crates. This training facilitates working with these animals and reduces the need for stressful and potentially injurious captures.

Will the Animal Be Caught in Water or on Land? The habitat is assessed to determine whether staging the capture on land or in the water is best and safe. In many enclosures land surface is insufficient or too crowded with vegetation and furniture to allow a well-coordinated capture. Similarly, some water features make it difficult to gain access to the animal. If the plan is to catch in the water, will the staff be on shore or down in the pool or both?

The characteristics of any water feature must be known to make a proper assessment of its utility in catching an animal. Important variables to know include: total pool area; the water depth; whether the water can be lowered without emptying the pool; the slope of pool sides; and whether staff can easily get out of it.

Land capture requires sufficient space for both the team and the animal, and must allow the staff to stay safely outside the strike zone. If the animal is on land, the plan should include a contingency for capturing it in the water. Unless caught immediately, crocodilians will seek refuge in water. If either land or water offer ample opportunity for capture, consider choosing to catch in the water. On land, crocodilians feel threatened and cornered. Water is a natural refuge and they often lay more passively, allowing easier placement of the rope and positioning of personnel.

Where Will the Animal Be Restrained? In some situations the crocodilian is removed from the enclosure to provide enough space to safely work around the animal. In other situations, the jaws are secured while the animal is in the exhibit, and then it is removed from the habitat before full restraint or loading into a crate.

Are Other Animals Present? Other crocodilians obstruct access or pose a significant and potentially

serious threat to staff and the animal to be captured. If possible, these animals are shifted out of the way before beginning. Additional staff may be needed to fend them off during capture; these animals may become involved as the animal and catch team move about the enclosure. The heightened stress or anxiety in the enclosure associated with the capture may cause these animals to strike out. Care must be taken to avoid injury to the animal being caught up and the staff members involved.

Animal Assessment

Not all techniques are appropriate for all species or size class. It is useful to have knowledge of the animal to be captured; crocodilian species are known for differences in temperament and their capabilities. Saltwater crocodiles (*Crocodylus porosus*) and Cuban crocodiles (*C. rhombifer*) are especially dangerous; they may charge and are powerful and agile jumpers. However, this does not imply other species are less dangerous. There are also individual animal differences; some usually mildmannered species can be unexpectedly belligerent. Ideally, all crocodilians are approached with the same degree of caution. There must be a healthy understanding and respect for the physical abilities of these animals.

Other aspects of the animal's biology, particularly snout morphology, are also considered when preparing for a capture. Slender-snouted species are more prone to serious snout damage during capture than are species with broader, more robust snouts. As a result, special precautions are necessary in preparing for capture of these more fragile species. Protecting the jaws prior to capture with cable straps may reduce disfiguring injuries. Conversely, exceptionally robust or broad snouted species (e.g., the broad-snouted caiman, *Caiman latirostris*) are often difficult to safely secure because there is relatively little purchase area for hands or mouth poles.

The "toothiness" of the animal to be captured is noted. Protruding teeth cause damage, or even serious injury, when accidentally caught on a hand or arm or forcefully slammed into a team member during a struggle. This danger persists even after the jaws have been secured. Many captive crocodilians have abnormal tooth development, resulting in misaligned teeth protruding from the jaws. In some species (e.g., the false gharial, *Tomistoma schlegelii*) the teeth are long, slender, sharp, and naturally interdigitating, making them very difficult to handle. In these animals it is necessary to wrap the entire jaw line in tape, or with a bath towel, rubberized shelf mat, or other material to prevent injury.

CAPTURE AND HANDLING BASICS

Strike Zones

The crocodilian head is its most dangerous part. Many people unfamiliar with these animals believe the tail is

the main area to be avoided. Although it is true that the tail can cause injury, it is the head that has a mouth full of 70 to 80 teeth and a very high bite force.

The stocky body form and heavily ossified skin of crocodilians limits their flexibility. However, they can and will strike sideways with exceptional speed. In most crocodilians laying on the ground the strike zone is defined by the arc of the head swinging from side to side. Therefore, it is much safer to approach an animal, secured by a rope around its neck, from the front than the side.

In the process of swinging its large, massive head rapidly to the side, a crocodilian generally swings or slaps with its tail. The tail is solid and strong and can knock a person off his or her feet or toward the jaws. Consequently, the tail arc must also be avoided by catch personnel.

Roping

Captures generally begin with the securing of a snare or rope noose to the animal. There are two basic variations of this procedure.

Neck Noosing This technique involves placing the rope over the head and cinching it around the neck. It is usually used for alligator, caiman, and heavy-bodied crocodiles. These animals have fairly large jowls at the back of the head, behind which the rope noose can take hold. Crocodilian necks are thick, heavily muscled, and usually capable of enduring without injury the forces that occur during struggling. In captivity, where it is often possible to carefully place the rope before closing the noose, some prefer to also hook the noose under one forelimb so it does not cinch tight around the neck. This technique is necessary in very large, heavy specimens that have to be pulled up and over a steep bank or the lip of a pool. This is to prevent too much force being applied to the neck and spine.

Top-Jaw Noosing Top-jaw noosing is used in species with body profiles too slim to allow a neck noose. The rope is caught in the teeth and held firmly. It is of a narrower diameter (less than or equal to 1.3 cm, 1/2 in.), allowing it to bind more closely around the upper jaw.

A clear advantage of this technique is the greater control of the head, since there is restraint of the snout. However, a major disadvantage is that when the crocodile jerks, twists, or shakes, which they do with tremendous force and speed, all of the forces are transmitted through the rope into the hands of the holder. Those who use top-jaw noosing usually secure the jaws with a narrow rope. Two people stand on either side of the head, outside of the strike zone, with the rope stretched between them. This is placed under the lower jaw, and then the ends of the jaw rope are wrapped around one another and exchanged. As the rope is pulled, the jaws are forced together. One person then steps in and holds

the knot while the second ties a securing knot. A safer alternative is the use a mouth pole.

Securing the Jaws

Depending in part upon the size of the crocodilian, the jaws can be secured with a variety of materials.

Tape Once the jaws have been closed (by hand in very small specimens or a mouth pole in larger animals), their jaws are usually taped. The standard used on larger crocodilians is silver, fabric duct tape. It has reasonably good adhesion to itself, but animals otherwise unrestrained are usually able to work it off of their jaws within a few hours. A major advantage is it has very little stretch, making it difficult to apply too tightly.

This author uses black PVC electrician's tape to secure the jaws of crocodilians less than or equal to 3 m (10 ft) for short periods of time. It is very quick to apply and sticks well to itself. Most other tapes do not adhere well to crocodilians, especially when wet. During application the tape must be wrapped around the snout and taped to itself to provide a good hold. A general rule is one wrap of electrical tape for each foot (0.3 m) of animal (i.e., for a 5-ft or 1.6-m alligator, wrap the tape around the snout five times).

Do not leave a crocodilian taped for more than or equal to a few hours. Electrical tape has a lot of stretch and can be applied with enough force to block blood flow to the skin. If it remains in place for too long it will cause ischemic skin damage, resulting within a few days in scabbing, sloughing, and scarring.

The author has also used the heavy, bright red, tape used for drywall seams. This has excellent adhesive force and a small amount of stretch. However, it does not tear readily making it necessary to cut with a knife. The great advantage of this tape is that it is highly visible making it immediately obvious when an animal has thrown its tape and its jaws are unsecured. This is an added safety measure, especially when transporting several animals at once.

Always create a tab when taping an animal; fold back the end so that it is easy to see and grasp. This facilitates removal of the tape during the release.

Cable Straps Cable straps (zip-ties) are frequently used on slender-snouted species (e.g., *Tomistoma*, *Gavialis*, *Crocodylus intermedius*, *C. johnsoni*). There is an increased risk they will damage or even break their snout/lower jaw during capture. This often happens when the animal bites on something in the exhibit and then roles, applying torsion to the jaws. Securing the jaws shut before a capture reduces the chances of injury. The captures also move more rapidly; staff can restrain the animal in a shorter period of time, further reducing chances of injury.

To use cable strap first make a noose by inserting the tip of the strap through the locking mechanism. Then,

drill or punch a small hole through the tip of the strap and thread a string, wire or monofilament line through and tie it. The string and the tip of the cable strap noose are then run through a length of 0.6- (1/4-) to 1.3-cm (1/2-in.) PVC pipe to serve as a catch pole. The noose can be accurately placed over the jaws without touching them. A rapid tug on the string will close the noose and pin the jaws shut, often without disturbing the animal. Alternatively, the cable strap noose is suspended from the string and lowered into a position around the jaws. A swift jerk tightens the strap around the jaws.

This technique is also used with other crocodilian species, but it is more difficult to zip-tie the jaws of broad snouted species. However, in many species there is a notch or depression in the jaw (e.g., behind an enlarged tooth) into which the cable strap can take hold and tighten down onto the snout.

Caution must be used with nylon straps. Do not trust them; they often are not affixed tightly and can easily slip, releasing the jaws. They also become more brittle with time and prone to breakage; buy new ones before each capture.

Other Binds Less frequently, jaws are bound with rubber bands or heavy cord. Strong, heavy, rubber bands made by cutting tire inner tubes into rings can be used for animals less than or equal to 3 m (10 ft) in length.

Eye Coverage

Cover the eyes whenever restraining a crocodilian. Use an eye cloth or, if the animal is fully restrained, cover with your hand. During a capture drop an eye cloth in place with a hook. This prevents the animal from seeing your movements, makes it less likely the animal will become unruly, and prevents the animal from directing a strike toward a capture team member. Covering the eyes also keeps the animal quieter and may reduce the stress of the experience for the animal.

Go to the Bathroom

There is no delicate way to state this and it seems an odd thing to mention in a discussion of catching crocodiles but, before beginning any major catch-up operation, make sure each person on the catch team has visited the restroom. These operations can be time-consuming and tense for the staff involved. The necessities of bodily functions can arise, making a team member uncomfortable and distracted. This can result in actions being rushed or mistakes being made.

CAPTURE AND RESTRAINT

Hatchling/Juvenile (less than or equal to 1 m)

Hatchling and small juvenile–sized crocodilians can still inflict a painful bite, so caution is still necessary when working with these animals. Biting a keeper is also stressful to the animal and may damage teeth or jaw

structures. Also, the animals are small enough that no matter where you grab them, you are never very far from the mouth.

This size animal is easily grasped by hand. Approach from behind and grab and hold firmly by the neck, over the shoulders, or on the front half of the torso (Figure 17.3). To reduce the chance of a bite use a hook, small stick or rod, or even a broom to push the head away from the hand and block as the animal is picked up. Pillstrom tongs, a standard tool for most herpetologists (see Chapter 20), do not work well with crocodilians. The bony armor on the neck and dorsum prevents the tongs from gaining a firm purchase, and the animals can twist, roll, and wrest themselves free. There is also a natural tendency to squeeze the tongs more firmly to prevent this, resulting in injury to the animal.

Once the animal is in hand the jaws must be secured. The animal is held firmly around the neck with one hand, and the other hand is advanced from behind, keeping it close to the body. It is placed around the neck and slowly slid forward while gently squeezing. As it moves up onto the head it will slowly close the jaws. The eyes are covered and the head held with this hand. The jaws are then secured shut with tape (even transparent tape will work on this sized animal, a rubber band, or a short length of cotton clothes line) (Figure 17.3).

Subadults (less than 2 m)

Subadult crocodilians or adults of smaller species (e.g., Chinese alligator, *Alligator sinensis*; African dwarf crocodile, *Osteolaemus tetraspis*; both species of the caiman genus *Paleosuchus*) are perhaps the most difficult size class to capture and handle safely. These animals are large and powerful enough to provide a great struggle, yet still agile and quick enough to turn rapidly and snap.

The tool of choice for these animals is the catch pole made by running a loop of rope through a length of PVC



Figure 17.3. Physical restraint of a small crocodilian (Crocodylus mindorensis). Note the electrician tape placed around the jaws and the hand grasping the neck and forelimbs.

pipe. The loop is placed over the animal's head and around the neck and pulled tight. The rope is bent back against the PVC pipe for added friction. PVC does have some flexion, so the animal is not completely controlled. However, the animal can easily be dragged and positioned with this device. Greater control of the animal is achieved if a second person grabs the tip of the tail and pulls the animal. This stretches the animal between the catch pole and second handler. Maintaining pressure on the tail prevents the animal from twisting or turning to bite. A mouth pole is used to close and secure the jaws. With the animal still controlled by the catch pole, the mouth pole is placed over the snout and the rope pulled tight. It is preferable to stand at the side and slightly behind the animal's head when doing this. The jaws are closed with pressure applied by pulling the rope. When the jaws are completely shut, the mouth pole is twisted several times to add pressure to the jaws. When the jaws are secure and the mouth pole is holding, another crew member steps in and tapes the jaws.

Adult (greater than or equal 2 m)

Capture and restraint of larger crocodilians is as much a matter of manpower and logistics as it is of proper procedure and safety. A sufficient number of staff is a necessity for a safe and efficient operation. Two people are plenty for a 2-m (6-ft) specimen. Generally, it is best to have at least three or four team members for a 2.5- to 3-m (8- to 9-ft) animal. Four or even more people are needed for specimens greater than 3 m (10 ft).

Not to belabor the point, it is ideal for working with these large specimens that they be trained to shift and, even better, into a crate. This provides substantial daily or weekly safety benefits to keeper staff and removes most of the trauma and anxiety of a physical capture. If this is not an option, or if the animal fails to shift when needed, than one may have to proceed with a capture.

As described, before beginning capture of a large crocodilian make sure ropes that are not frayed or worn, and have been soaked are available. Wet ropes not only sink better to position them around an animal, but they do not burn the skin of the animal as dry ropes often do during a struggle.

Catching Adult Crocodilians in Water If the plan is to catch the crocodilian in the pool, the following are some suggestions for techniques to use. If it is possible to lower the water, drop it to a level that just covers the back of the animal (approx. 25 cm, 10 in.). This depth limits the animal's mobility within the water feature while still allowing it to submerge its head. It also provides better visibility of the animal and any obstacles. It is important to keep enough water in the pool for the animal to remain submerged. As long as it can keep its eyes underwater, it is much less likely to become violently defensive.

There are various means of securing an animal in this situation. Most commonly, a rope is placed around the head and neck, and possibly one of the forelimbs. Hooks greatly facilitate safe rope placement and positioning of the noose. Alternatively, a wide lasso is thrown over the head, or a breakaway noose or a cable snare catch pole are used to get a line on the animal. If the animal is slender snouted, or there are many obstacles in the environment on which the animal might injure itself, the jaws are first secured with a cable strap.

If the team is familiar with the temperament of the animal and it is not reacting violently, it is often possible to manipulate the animal when the water is shallow. Large nets or marine mammal slings may be used to slide under the animal, envelop it, and lift it out of the pool area, greatly reducing the animal's struggles and chances for injury. Animals may also be able to be pushed or herded into a crate or large-diameter PVC pipe that has been placed in the pool (Saumure et al., 2002).

A common disadvantage of catching in the water is that most pools are hard sided. They are generally constructed of concrete or gunite and readily damage the side of the head of a struggling crocodilian. Attempt to keep the animal away from the pool sides as it struggles, and move it past these structures as rapidly as possible. Sealed foam rubber gym mats or other shock-absorbing materials can be placed against the side of a pool to protect the animal.

Catching Adult Crocodilians on Land Once the rope is placed on a crocodilian on land, there will be a struggle. They are able to generate a tremendous amount of resistance with their short legs forced into the ground. It is best to have sites already identified where one can tie off the rope (fence posts, trees, etc.). Trees must be of sufficient diameter to resist the force of the animal; larger crocodilians will uproot a small tree. Tying off the rope restricts the animal's movements, facilitates repositioning of the handlers to provide further restraint and, perhaps most importantly, saves energy. Tired or exhausted catch crews are more likely to make mistakes. Successful techniques used for capture of crocodilians on land include the following.

The use of a rope to secure a hold on the animal is most common. Rope lassos can be tossed over the head or the rope is placed with a hook or catch pole. Once the rope is secure, the crocodilian is pulled to the designated work area. The animal is tied to a tree or post. Most carefully prepared capture plans unravel when the crocodilian begins to roll. This tangles ropes, scatters equipment, moves the animal into areas that compromise it or the catch staff and, generally, messes up an otherwise well-organized process. Catch leaders must recognize and concede when a plan has been disrupted. Most often it is best to pause momentarily, regroup, reorganize, and then begin again. Once an animal is tied off, it may be possible to cinch a second rope to the tail.

Stretch the animal and tie off the second line. This may help prevent the animal from rolling. Once the animal is restrained, a mouth pole is used to close and secure the jaws.

If there is a tree or post within the area, try to pull the animal up to it so that the head is pulled up against the tree. This acts as a stubbing post and can greatly restrict the movement of the head, making it safer to work around the animal.

Most crocodilians, when roped, will pull against the rope in an attempt to escape. A few may be more bold or aggressive and lunge at the staff on the other end of the rope. If this appears to be a potential, either control the animal by catching it up with a rigid catch pole, or place a second rope over the head and stretch the animal between them.

Mounting There are situations in which it is necessary to straddle over or "mount" a large crocodilian. With caution, procedure and experience, this is a fairly safe technique. However, the level of security it offers personnel is much less than that of other methods recommended in this chapter (i.e., shifting, working at a distance with hooks and poles, or physical restraint on a backboard). If any of these other methods satisfy the purpose, use them instead.

Mounting allows one person to control the animal and its head, take blood or other samples, and facilitates measurement. Once in position on top of the animal, the handler is relatively safe. Even with vigorous twists from side to side, the animal should be unable to bite. Care is taken to prevent the animal from rolling. The best technique to prevent this is for other catch crew to keep the tail straight and pull the hind limbs back and off of the ground. Some species (especially caiman) are quite capable of and prone to snapping their heads straight up as a handler leans over them. This is extremely dangerous and can cause serious injury; sit up straight while straddled on the animal.

To attain this position the handler must move into the animal's strike zone, hence the danger of this technique. To do this safely, the animal must be tightly roped and the rope tied securely in front of the head. This prevents the animal from twisting back on the restrainer. The handler moves up along the axis of the animal's body, essentially straight up the tail and the back. Stay as close to the body as possible. If the animal thrashes unexpectedly, this will reduce the impact and help maintain your balance. The author finds it useful to nudge the animal with his foot before he proceeds. This tests whether the animal is ready to burst into a struggle. When ready to mount, move forward quickly and deliberately. Place one foot against the base of the tail just behind a hind limb. Move forward rapidly, place the other foot against the other side of the torso at midbody and quickly drop into a seated position on its back, with knees planted behind the forelimbs of the animal.

Cover the eyes with your hand, and keep your other hand on the top of the head and snout. Do not let fingers trail off the side of the face as this might elicit a snap to the side.

When ready to "dismount," make sure the path behind is clear and quickly step back off of the animal in the same manner you approached; place your feet against the body and step back along the body axis.

RESTRAINT AND TRANSPORT

Once the crocodilian is captured and the jaws safely secured, the techniques for safely and efficiently moving it vary. The method of transport depends, obviously, on the size of the specimen and the distance it must be transported. For transport within the institution, smaller specimens are simply carried or placed in a bag, pillow case, duffel bag, bucket, or ice chest. However, even small crocodilians can deliver a painful slap with the tail. This is prevented by placing the tail underneath the arm while holding the animal around the neck and supporting its weight on your arm.

Larger specimens can be heavy, at least unwieldy if not often combative, and difficult to lift and carry. There is a natural tendency to try to lift these specimens by their legs. This can be injurious and must be avoided. The shoulder and hip joints of crocodilians are relatively shallow. It is not difficult to pull a limb out of the joint when lifting its leg. If an animal must be lifted, reach underneath and support it from below the torso and tail. However, crocodilians are not accustomed to being off of the ground; they will often struggle, twist, and attempt to roll. The head must always be controlled. Even with the jaws taped shut, it is dangerous. Always keep it directed away from others and keep your head away from it.

Ideally, larger crocodilians are either placed into a shipping crate or strapped to a backboard, platform, or aluminum ladder for transport (Figure 17.4). They must be thoroughly restrained to prevent them from struggling to free themselves and potentially injure themselves or the capture team. Although harsh, it has many benefits to the animal as well as to personnel. Some crocodilians continue to struggle for long periods after capture. This increases their stress and exhausts them. Very large saltwater crocodiles (Crocodylus porosus) are known to struggle to such an extent that they build up dangerously high levels of lactic acid in their bloodstream (Seymour et al., 1987). This can result in severe acidosis and death. Crocodilians that are completely restrained on a board or platform usually cease to resist. Without the continued struggle there is little chance of the animal seriously compromising itself physiologically.

Restraint can be in the form of nylon cable straps (for smaller specimens), ropes, or cargo straps. The platform can be lifted easily and can be placed on a cart or truck for transport. Straps are placed in several places along



Figure 17.4. Physical restraint of large crocodilian (Crocodylus novaeguinae) with a restraint board. Cargo straps are used to tie the animal to the board. A towel covers the eyes to reduce struggling.

the body: over the neck, across the shoulders just behind the forelimbs, across the center of the torso, just in front of the hind limbs, on the base of the tail just past the pelvis, and one or more wraps across the anterior half of the tail (Figure 17.4). The head is also secured. If the animal is restrained on an aluminum ladder, it is possible to run the rope through the hollow rungs of the steps to completely secure it to the structure. Cargo straps can be purchased in a variety of widths and strengths. It is best to use those that have a wrenching action to tighten the strap after it is attached.

It is possible to physically restrain even the largest of crocodilians in this manner, assuming the platform and straps are sufficiently strong. However, it can be difficult to release the grip on the buckle of very large cargo straps. A heavy hook is useful for this purpose. For transport to other institutions, crocodilians are generally confined to a shipping crate.

RELEASE TECHNIQUES

Releasing an animal that has been captured poses as many safety concerns as the initial capture. One must be concerned not only with the safety of the staff, but also with risks to the animal being released or its enclosure mates.

There is a real possibility the animal may attempt to turn and bite after its jaws have been unbound. Methods should be used to put distance between the catch personnel and the animal being released. One such method is the use of a jaw rope. A length of narrow rope is passed underneath the tape or rubber band holding the jaws shut. It is passed from the front to the back so there is no danger of accidentally causing the binds to slip and release the jaws prematurely. The rope is then tied off so that it will grip the binds. With the animal in position, all other restraints are removed, taking care not to trip on or accidentally pull the jaw rope. When all restraints are free, and all personnel are well away from the animal, a hard tug on the jaw rope will pull the bindings from the jaws, freeing the animal.

In cases in which the animal has been "top-jaw roped" it serves as the jaw rope. With the jaws still firmly taped or tied the noose of the top-jaw rope is opened. The length of rope still firmly held in the crocodile's jaws is then used to make several wraps around the snout. This then serves to secure the jaws while the other bindings are removed. When all other restraint are removed and everyone is safely away, the top-jaw rope is unwrapped from the snout. The animal will open its mouth and release the rope.

A rope noose catch pole or mouth pole is ideal for assisting release. The animal is restrained by the catch pole while the jaw bindings are removed. The pole prevents the animal from moving toward the catch team member holding it. When everyone is safely back from the animal the catch pole is removed.

Immediately after release crocodilians may be highly agitated. If there are other enclosure mates, there is a possibility of displaced aggression leading to injury of one or more of the other animals. Before releasing a crocodile make sure it is positioned at a distance from others.

If it is suspected that aggression will occur it is possible to release an animal with its jaws still bound and remove the bindings later. Re-tape the jaws and insert a piece of rope or a metal ring under the tape. The rope should float and have a large loop tied in its free end. Once the animals have had sufficient time to calm down after release, a long-handled hook is used to catch the loop in the rope or the metal ring and pull the tape from the jaws.

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18 Crocodilians (Crocodiles, Alligators, Caimans, Gharial)

Gregory J. Fleming

INTRODUCTION

Crocodilians represent one of the oldest living groups of reptiles and, because of their sheer size and character, are popular exhibit animals in zoos. Many of the 23 crocodilian species are endangered and conservation programs, in both zoos and in situ, are increasingly making demands for safe and effective chemical immobilization and anesthesia (IUCN Red Data Book, 1982).

PHYSIOLOGY AND ANATOMY

Crocodilians spend much of their time entirely submerged except for their eyes and nares. Each nostril acts as a waterproof valve that is closed with a muscular flap during submersion. Immobilizing agents that relax the muscles of the nostril obtund this reflex (Fleming, 1996). The soft palate and gular fold that protrudes from the floor of the mouth form an additional respiratory valve. The elongated soft palate presses down against the gular fold, allowing the submerged crocodilian to open its mouth without water entering the internal nares and glottis. The gular fold must be displaced ventrally to visualize the glottis for endotracheal intubation (Figure 18.1).

Crocodilians possess a pair of well-developed lungs. They do not respire through their skin and cloaca (Klide and Klein, 1973). The primary respiratory muscle groups are the intercostal and two transverse membranes, the post-pulmonary and post-hepatic. The latter are comprised primarily of fibrous tissue with a muscular component (Van der Merwe and Kotze, 1993). The post-pulmonary membrane separates the lungs from the liver. The post-hepatic membrane is attached to a sheet of muscle that inserts at the os pubis. These membranes act as a diaphragm. Ventilation is achieved by expansion of the intercostal muscles. The membranes then pull the liver in a caudal direction to create negative

pressure in the lungs. The lungs expand and air is drawn in through the nostrils. The glottal valve is then closed, holding the air in the lungs. Once the glottal valve relaxes, air is expelled passively via the elastic recoil of the intercostal muscles and the post-pulmonary/post-hepatic membranes and lung tissue.

Cardiovascular System

Crocodiles are the only reptiles that possess fourchambered hearts (Millichamp, 1988; Murphy, 1996). The heart functions as a mammal's with the exception of the foramen of Panizza, a small window located between the intraventricular septum at the confluence of the left and right aortic arches (Millichamp, 1988). This opening acts as a pressure valve, allowing blood to flow between the venous and arterial systems. This flow, from high to low pressure, results in venous admixture. When the animal is breathing, left ventricular pressure is greater, allowing a small amount of oxygenated blood to flow through the foramen into the venous blood supply (Millichamp, 1988). When the crocodilian submerges, air held in the lungs restricts blood flow through the pulmonary capillary beds, resulting in pulmonary hypertension that increases right ventricular and pulmonary arterial pressures. As a result blood flows from right to left through the foramen. Deoxygenated blood is diverted away from the lungs through the left aortic arch to organs that are less sensitive to hypoxemia (e.g., liver and stomach) (Grenard, 1991). Oxygenated blood is diverted to oxygen-dependent organs (i.e., the heart and brain). A combination of blood shunting and anaerobic metabolism may allow an inactive crocodilian to stay submerged for 5 to 6 hours (Lane, 1996). This right-to-left shunt through the foramen of Panizza may have clinical implications during anesthesia when the crocodilian does not have ventilatory support or is apneic. Shunting of blood away from the lungs delays inhalant anesthetic uptake and removal, emphasizing the importance of assisted ventilation.



Figure 18.1. View of the gular fold, of a Chinese alligator (Alligator sinensis), being depressed with a tongue depressor to access the glottis. Note the oral speculum constructed of a piece of PVC pipe wrapped with tape (Courtesy of Dr Maud LaFortune).

Renal Portal System

Crocodilians possess a renal portal system composed of the renal portal vein arising from the epigastric and external iliac veins (Millichamp, 1988). These vessels drain blood from the dorsal body wall, cloaca, sex organs, and bladder. Theoretically, drugs injected into the caudal half of the body, base of the tail, and hind legs may be cleared by the kidneys prior to reaching the systemic circulation. However, this does not appear to be clinically significant (Millichamp, 1988).

Physiological Reference Ranges

Obtaining heart and respiratory rates is very difficult in awake crocodilians. In one study, juvenile American alligators (Alligator mississippiensis) and smooth-sided caimans (Caiman sclerops) were implanted with monitoring equipment and isolated from human contact for 12 to 20 hours before measuring cardiac and respiratory rates. Normal respiratory and heart rates at 22°C were 0.6 and 11.6 breaths per minute, and 1.6 and 14.2 beats per minute, respectively. Following visual contact with humans, both heart and respiratory rates doubled to 30 beats per minute and 6 breaths per minute (Huggins, Hoff, and Pena, 1969). Consequently, most restrained crocodilians are likely to be tachycardic and tachypneic. In general, heart and respiratory rates vary inversely with the size of the animal, but are affected by environmental temperatures. In Nile crocodiles (Crocodylus *niloticus*), heart rates increased as temperatures increased, from 1 to 8 beats per minute at 10°C up to 24 to 40 beats per minute at 28°C. Prolonged exposure to high temperatures above 40°C is potentially lethal because of tissue damage. Heart rates as high as 55 beats per minute at 29°C have been recorded in Nile crocodiles caught in traps (Loveridge, 1979).

Thermoregulation

Crocodilians are poikilothermic, regulating their body temperatures by using external environmental heat sources. Given a range of environmental temperatures, they are able to select the preferred optimum body temperature (POBT) for their metabolic needs. For captive crocodilians, a recommended range is 25 to 35°C (Bennett, 1996). Temperatures below and above POBT interfere with digestion and immune function. American alligators take twice as long to digest food at 20°C than 28°C, whereas smoothsided caimans digest food three times faster at 30°C than 15°C (Diefenbach, 1975; Coulson and Hernandez, 1983). However, experimental infection of American alligators kept at 30°C demonstrated the greatest white blood cell response to infection and survival, whereas alligators held above the POBT at 35°C succumbed to infection in 3 weeks (Glassman and Bennet, 1978).

Anesthetized crocodilians should be kept at temperatures near their POBT or around 30°C (Bennett, 1996). Environmental temperatures below POBT decrease metabolism and thereby prolong clearance of injectable drugs, resulting in delayed recoveries. Induction may also be prolonged because of slowed absorption and circulation times. For example, large Nile crocodiles induced with the neuromuscular blocker gallamine took twice as long to become recumbent at 14°C (40 minutes) compared with 26°C (20 minutes) (Fleming, 1996).

RESTRAINT TECHNIQUES

All crocodilians are capable of inflicting serious damage by ether biting or lashing out with tails. For this reason, a number of restraint techniques have been developed for wild and captive crocodilians (Wallach and Hoessle, 1970; Loveridge and Blake, 1972; Walsh, 1987) (see Chapter 17). The goal of physical restraint is to be able to administer injectable anesthetics quickly and safely. Successful restraint must be safe for both the handlers and the animal. Reported injuries associated with physical restraint include fractured bones, damaged eyes, and drowning (Walsh, 1987). Prolonged struggling results in marked lactic acidemia, with pH levels dropping to 6.6 to 6.8 (normal range, 7.2 ± 0.2). Like other reptiles, crocodilians take a prolonged period of time to recover from elevations in lactic acid (Seymour et al., 1987). Captured crocodilians may become unconscious and drown if not allowed to rest after prolonged physical restraint (Sedgwick, 1986). A variety of capture techniques have been described using scoop nets, squeeze cages, tongs, harpoons, rope traps, snares, box traps, and tubes, all with varying success (Wallach and Hoessle, 1970; Fowler 1985, 1986; Blake, 1993; Jones and Hayes-Odum, 1994) (see Chapter 17).

DRUG DELIVERY

The goal is to get close enough to the animal to administer the anesthetics safely. In most cases, this entails using injectable agents.

Darts

Darting can be an effective method of delivering immobilizing agents (see Chapter 4). However, this delivery route has several major disadvantages in crocodilians: (1) it is difficult to get an accurate shot while the animal is in the water; (2) it is difficult to determine dart discharge; (3) the osteoderms covering most of the dorsal surfaces may deflect the dart; and (4) once the animal is darted, it may submerge and drown. For these reasons, darts are rarely used in the field (Flammard, 1992; Blake, 1993). In captivity a dart is an appropriate drug delivery method in controlled situations (i.e., a dry enclosure).

Hand Syringe

The hand syringe has the advantages that it can be accurately placed and the rate of injection can be controlled. However, the animal must be secured for safe injection. This technique can be used for smaller crocodilians that are restrained and for administering reversal agents to larger animals. Both intramuscular and intravenous routes can be used as described in the following.

Pole Syringe

The advantage of a pole syringe is that crocodilians can be injected while unrestrained in a shallow pool, net, or a snare. The main disadvantage is that the injector must be within 2.5 m of the animal, and injection volumes are limited to 10 to 15 ml. If the anesthetic agent is not administered fast enough, the pole syringe and handler will be damaged by the animal.

Injection Sites

The base of the tail, just caudal to the hind legs, is a common area for intramuscular injection. This area is composed of many layers of muscle, with the vertebrae located deep within the muscle. There is no risk of injection into any internal organs. In obese animals there may be a layer of fat that, if injected, could delay drug absorption. Care must be taken to direct the needle between the scutes to assure complete drug delivery. The hind limb muscles can be used for injecting smaller animals and to give reversal agents (Jacobson, 1984; Bennett, 1996). Intravenous injections are best accomplished by accessing the ventral coccygeal vessels. This site can be used to obtain blood samples, inject intravenous drugs, or place intravenous catheters (Wellehan et al., 2004) (Figure 18.2).

Handling

Once the immobilizing drug(s) has taken effect, it is prudent to use a pole or stick to stimulate the crocodilian a

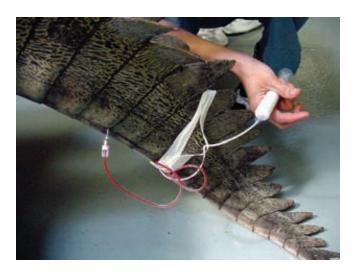


Figure 18.2. Intravenous injection in a gharial (Gavialis gangeticus) using the lateral approach to access the ventral coccygeal vessels. The needle is inserted at a 90°-degree angle at the lateral midline of the tail, just beneath the lateral spinous process of the vertebral body. This same approach may be used to complete intravenous injections of anesthetic drugs such as propofol (Courtesy of Dr. Maud LaFortune).

number of times to ensure there is no response. Once this is accomplished, the eyes are covered with a damp towel and the jaw taped shut. Care is taken to avoid taping over the nostrils.

The crocodilian can then be rolled onto a stretcher or large tarp. Large crocodilians may weigh up to 500 kg and pulling on legs, to move them or lift them, may result in fractures or luxations (Blake, 1993). To lift a crocodilian out of shallow water, 1-m lengths of flat 6-cm commercial crane slinging can be placed under the chest and hind legs. The slings allow the animals to be easily picked up and moved without pulling on the legs (Fleming, 1996).

If the animal is to be intubated, a mouth gag, made of a steel ring, polyvinyl chloride (PVC) pipe, or a wood block should be used to prop open the mouth. Depending on the size of the animal, steel tubing (in varying diameters and widths) can be cut and wrapped with several layers of tape or leather so as not to damage the teeth. A hole in the middle of the gag allows for the passage of anesthetic tubes or endoscopic equipment (Figure 18.1).

MONITORING

Physiological monitoring can include the use of stethoscope, pulse oximeter, Doppler blood flow transducer, electrocardiography (ECG), and ultrasound or blood gas analysis (see Chapter 6). Anesthetic depth is evaluated using the limb withdrawal reflex, cardiac rates, righting response, and bite and corneal reflexes (Neill, 1971; Bennett, 1996; Heaton-Jones, Ko, and Heaton-Jones, 2002).

The electrocardiogram and reference values have been described for the American alligator (Heaton-Jones, 1996). The ECG leads are attached to 2.5-cm needles passed through the skin. Although pulse oximetry may be used to assess heart rate, it does not appear to accurately calculate oxygen saturation in reptiles (Mosley, Dyson, and Smith, 2004). Skin thickness and pigmentation hamper measurement with the transmission probe, whereas a reflectance probe in the cloaca may improve the signal. Blood gas measurements in crocodilians are difficult to interpret because numerous variables such as temperature, feeding, and sample site (arterial, venous, or a combination of both) influence the results. American alligators have the ability to reduce the affinity of hemoglobin to reduce blood oxygen affinity at certain pH levels. This allows for more oxygen to be released from the hemoglobin under certain conditions, such as acidemia, increasing the total amount of oxygen available to tissues (Busk et al., 2000).

Doppler blood flow detection is a very reliable method of obtaining heart rate (Bennett, 1996; Neilson, 1996). The probe is placed over the heart or a large blood vessel such as the ventral coccygeal, brachial, or femoral artery. Blood flow in the optic arteries may be detected by placing the probe against the globe with the eyelid or third eyelid closed. Alternatively, a dorsally directed probe placed in the cloaca may detect arterial blood flow.

ANALGESIA

Information on the use of analgesics is limited (see Chapter 3). In juvenile saltwater crocodiles, the μ opioids morphine (0.8 mg/kg) and meperidine (pethidine) (2 mg/kg) showed evidence of analgesia when measured with thermal antinociception (Kanui and Hole, 1992). The use of meloxicam (0.2 mg/kg IM) has only recently been reported in reptiles (Whiteside and Black, 2004; Wellehan, 2006). This author has used meloxicam (0.1 mg/kg orally once a day for 14 days) in two adult Nile crocodiles with traumatic foot lesions. The day following treatment both crocodiles showed marked improvement in ambulation, with no evidence of lameness.

SEDATIVES

Diazepam hydrochloride (0.22–0.62 mg/kg) administered 20 minutes prior to succinylcholine resulted in a smoother induction and lower dosages in American alligators (Loveridge and Blake, 1972). Heart rates were decreased, respiration was maintained, and recovery for most was within 3 hours. The combination of ketamine and diazepam resulted in recovery times of 6 hours (Frye, 1991).

Reversal and Recovery Flumazenil has been used in dogs to reverse several benzodiazepines (ratio of 1:13,

flumazenil to diazepam, 1:20 flumazenil to zolazepam) (Terpin, Dodson, and Spotila, 1978; Lang, 1987) and may reduce recovery times in crocodilians. However, it is very expensive, making its routine use prohibitive, particularly in larger reptiles.

LOCAL ANESTHETICS

Local anesthetics are indicated for minor surgical procedures such as skin laceration repair or abscess removal (Jacobson, 1984; Burke, 1986). Toxic lidocaine dosages have not been established. A nerve locater can be used to accurately place local anesthetics (Wellehan, 2006). Nerve locators use a pulsatile electric current passed through a needle in contact with the motor nerve (e.g., mandibular) that innervates and thus stimulates an identifiable muscle (e.g., digastricus muscle). Local anesthetic (e.g., 2% mepivacaine, 1 mg/kg) injected down the needle blocks nerve conduction. This technique has been used to provide analgesia in the mandible of American alligators, dwarf crocodiles (Osteolaemus tetraspis) and Yacare caimans (Caiman yacare) (Wellehan, 2006) for tooth removal.

IMMOBILIZING DRUGS

Muscle Relaxants

Muscle relaxants do not provide analgesia for painful procedures, and auditory, visual, and tactile stimulation must be minimized (Huggins, Hoff, and Pena, 1969). They have been used historically in Africa for transportation and capture of wild crocodilians (Fleming, 1996).

Gallamine Triethiodide

This short-acting, non-depolarizing neuromuscular blocking agent produces flaccid muscle paralysis (Woodford, 1972; Loveridge, 1979; Flammard, 1992). Even though immobile, the crocodile is fully conscious and aware of auditory, visual, and tactile stimulation, which may result in tachycardia and tachypnea (Lloyd, Reichard, and Odum, 1994). The eyes should be covered and all external stimuli (i.e., noise) kept to a minimum. Gallamine may cause the mouth to open as the muscles relax, the Flaxedil (gallamine) reaction (Blake, 1993). Gallamine has been the drug of choice in South Africa for immobilization of Nile crocodiles for over 25 years in both the field and in captivity (Webb and Messel, 1977; Loveridge, 1979).

Wide dosage ranges (0.6 mg/kg IM in a 312-kg Nile crocodile to 4 mg/kg IM in a 9.7-kg crocodile) have been reported (Loveridge, 1979). In a study of 38 adult Nile crocodiles, the effective dosage was of 1 to 2 mg/kg IM (Fleming, 1996). Larger crocodiles (greater than 3 m) were immobilized with dosages of 1.1 mg/kg IM, whereas smaller crocodiles were immobilized with a dosage of 2 mg/kg IM. Gallamine overdosage may result in bradycardia, gastrointestinal hypermotility, increased

salivation, mydriasis, and respiratory muscle paralysis, leading to death (Blake, 1993; Lloyd, Reichard, and Odum, 1994). Faster induction times (i.e., 15–30 minutes) were reported with higher environmental temperatures (i.e., 30°C). Cuban crocodiles have also been successfully immobilized with gallamine (0.64–4 mg/kg IM) (Lloyd, 1999). The response to gallamine (1 mg/kg IM) in American alligators is variable and may cause death (Jacobson, 1984). Deaths in false gharials (*Tomistoma schlegelii*) have also been reported (Lang, 1987; Frye, 1991).

Crocodilians immobilized with gallamine recover within 12 to 24 hours without reversal. Recovery appears to result from renal excretion of the unchanged drug (Flammard, 1992). Farmed Nile crocodiles are routinely left without reversal in a shaded area, with no access to water for 24 hours, until they walk (Webb and Messel, 1977; Flammard, 1992). Accidental drowning may occur in partially recovered animals.

Neostigmine methylsulfate (0.03–0.06 mg/kg) competitively antagonizes the effects of gallamine in the Nile crocodile (Jacobson, 1984; Flammard, 1992; Fleming, 1996). Recovery occurs within 5 to 40 minutes, depending on dose and temperatures. Re-dosing is rarely necessary (Pleuger, 1973). It is advisable to reverse the crocodile several meters from water and allow it to get up and walk into the water to assure that it has recovered (Fleming, 1996). Side effects reported in mammals, but not crocodilians, include those of a cholinergic crisis (i.e., vomiting, diarrhea, salivation, and bradycardia) (Schumacher, 1996).

Succinylcholine Chloride

Succinylcholine has been used alone, or in combination with other drugs, for many years in numerous species (Loveridge and Blake, 1972; Klide and Klein, 1973; Jacobson, 1984; Spiegal et al., 1984; Millichamp, 1988; Flammard, 1992; Blake, 1993). American alligators greater than 1.5 m are immobilized at 0.4 mg/kg. Smaller alligators require a larger dose (1 mg/kg IM) with recumbency in 5 minutes and recovery in 1 hours (Jacobson, 1984). Higher dosages (3-5 mg/kg IM) also produce rapid recumbency within 4 minutes, but prolonged recovery (up to 7–9 hours) may occur (Brisaben, 1966). The combination of succinylcholine (0.37 mg/kg IM) and diazepam (0.24 mg/kg IM) successfully immobilizes adult American alligators (Loveridge and Blake, 1972). The diazepam administered 20 minutes before the succinylcholine reduces stress and the succinylcholine dose. All animals are completely recovered within 3 hours. Juvenile caiman (Caiman crocodylus) are immobilized at dosages of 0.33 to 2.2 mg/kg IM, with recovery in 5 to 40 minutes (Johnson, 1991).

Both freshwater (*Crocodylus johnsoni*) and saltwater crocodiles (*Crocodylus porosus*) have been immobilized successfully (Loveridge and Blake, 1972). Saltwater crocodiles require a higher dosage (2.2 mg/kg and

5 mg/kg) than freshwater crocodiles (0.8 mg/kg and 0.3 mg/kg at 5 and 35 kg, respectively). Dosage for both species is inversely related to weight. Immobilization is achieved at 5 to 7 minutes and up to three times the therapeutic dosage results in no deaths (Loveridge and Blake, 1972).

There is no reversal drug; recovery is dependent on metabolism and renal excretion (Pleuger, 1973). At preferred optimum body temperature, recovery takes 30 minutes to several hours, depending on the dose administered (Jacobson, 1984; Lloyd, Reichard, and Odum, 1994).

Atracurium Besylate

In American alligators, atracurium besylate (15 mg/kg IM) 15 minutes after diazepam (0.4 mg/kg IM) induced loss of righting reflex within 40 minutes and recovery by 6 hours (Clyde, 1990). Five of eight animals became severely apneic (less than 1 breath/minute), and were manually ventilated with room air for up to 5 hours. Neostigmine methylsulfate (0.05 mg/kg IM) and atropine sulfate (0.01 to 0.02 mg/kg IM) reversed the muscle relaxation induced by atracurium (Clyde, 1990).

OPIOIDS

Etorphine Hydrochloride

Effective dosage varies considerably between and within species. For example, American alligators (1.6–3.9 kg) required a dose of 1.3 to 3.1 mg/kg, whereas larger alligators (39.5–68.0 kg) required only 0.03 to 1.3 mg/kg (Hinsch and Gandal, 1969). American alligators (0.29 to 0.51 mg/kg IM) were immobilized within 20 to 25 minutes and recovered in 60 to 180 minutes with no reversal drug (Hinsch and Gandal, 1969). A caiman (0.11 kg) administered a high dosage (44 mg/kg) was immobilized at 11 minutes and recovered by 40 minutes (Thurmon, Tranquilli, and Benson, 1996). Intraperitoneal administration is effective, reducing induction times while having a similar duration of effect compared with IM administration. However, in Nile crocodiles, dosages as high as 8 mg/kg IM were ineffective and only produced pupillary dilatation (Loveridge, 1979).

Without administration of reversal drugs, crocodilians recover within 1 to 3 hours (Lang, 1987). There is no report of using either naloxone or naltrexone to reverse etorphine.

DISSOCIATIVE ANESTHETICS

Ketamine Hydrochloride

Ketamine alone is variably effective. It has been used to anesthetize spectacled caiman (44–50 mg/kg), juvenile American alligators (11–12 mg/kg, 1-hour induction) (Beck, 1972; Stoskopf, 1993), and adult American alligators (45–70 mg/kg, 20 min induction)

(Stoskopf, 1993). In American alligators a high dosage (50 mg/kg) was effective, whereas a lower dosage (30 mg/kg) had variable effect (Loveridge, 1979; Heaton-Jones, 1996). Ketamine (18–45 mg/kg) in Nile crocodiles had little effect, whereas higher dosages (59–110 mg/kg) caused death in three animals (Loveridge, 1979). Very high dosages (around 110 mg/kg) in other reptile species cause bradycardia and respiratory arrest requiring intubation and positive pressure ventilation to assist recovery (Burke, 1986; Bennett, 1996).

There is presently no reversal agent, and recovery times are dosage dependent, taking up to several hours (Bennett, 1996).

Tiletamine/Zolazepam

In American alligators this drug combination (15 mg/kg IM) did not produce complete immobilization (Jacobson, 1984). Palpebral reflexes were unaffected; hind limb withdrawal was slow and episodes of paddling were noted. Righting reflex was achieved 3 hours post-injection. However, higher dosages prolong recovery.

Partial reversal has been reported using flumazenil (1 mg/20 mg of zolazepam) (Lang, 1987). It is seldom used because it is very expensive, and reversal of the combination may "unmask" the adverse effects (e.g., seizures) of tiletamine.

BARBITURATES

The first reported use of pentobarbital (200 mg/kg PO, followed by 15 mg/kg IP) was in a Nile crocodile for removal of a gastric foreign body (Page, 1996). In the same species pentobarbital (28 mg/kg) produced immobilization in 2 hours, with recovery extending to 12 days. A high dosage (53 mg/kg) caused death (Loveridge, 1979). When administered to spectacled caiman (8.8–15.4 mg/kg IM) induction times were 30 to 45 minutes and recovery occurred within 1 to 5 days. Therefore, the use of pentobarbital is not recommended since there are many safer available alternatives.

α-2 ADRENERGIC AGONISTS

Xylazine has variable effects in Nile crocodiles; used alone (3–11 mg/kg) it has no effect. A combination of xylazine (1–2 mg/kg IM), followed 30 minutes later by ketamine (20 mg/kg IM) resulted in effective surgical anesthesia for 50 minutes with a 3- to 4-hour recovery (Idowu and Akinrinmade, 1986).

Medetomidine (131–220 μ g/kg) has been used in American alligator in combination with ketamine (7.5–10 mg /kg) (Heaton-Jones, Ko, and Heaton-Jones, 2002). Juvenile alligators required the higher dosages. Mean induction times for juveniles and adults were 19.6 and 26.6 minutes, respectively. Total anesthesia times were 61 to 220 minutes, with any procedure over

120 minutes receiving supplemental inhalant anesthesia. Medetomidine (150 μ g/kg) produces bradycardia and bradypnea (Smith, McGuire, and Mitchell, 1998; Smith et al., 1998a,b).

Yohimbine (0.1 mg/kg IM) reverses the effects of xylazine. If reversal agents are not used, recovery times are variable depending on dose, and may last 3 to 12 hours (Lang, 1987; Frye, 1991). Medetomidine is reversed with atipamezole (five times the dose of the medetomidine IM). Reversal times vary with dosage and body temperature. In alligators recovery was achieved in 35 to 37 minutes (Heaton-Jones, Ko, and Heaton-Jones, 2002).

OTHER INJECTABLE AGENTS

Tricaine Methane Sulfonate

Tricaine methane sulfonate (MS-222) (88–99 mg/kg IM) in juvenile American alligators produced immobilization in 10 minutes and prolonged recovery times of 9 to 10 hours (Brisaben, 1966). A higher dosage (150 mg/kg) anesthetized an alligator for 30 hours (Coulson, Hernandez, 1983). Tricaine has also been used in spectacled caiman (110 to 154 mg/kg IM) with no effect (Johnson, 1991).

Propofol

Propofol is an excellent induction agent; a single injection may give 15 to 25 minutes of anesthesia, with righting reflexes returning after 25 to 40 minutes. It can also be used as a continuous infusion to maintain surgical anesthesia (Divers, 1996; Schumacher, 1996). Its major disadvantage is that it must be injected IV, limiting its use in large crocodilians unless they are restrained. Although dosages in reptiles of 10 to 15 mg/kg IV have been reported, it is the author's opinion that dosages as low as 5 mg/kg IV may be enough to allow for intubation in many crocodilian species (Dennis and Heard, 2002). A butterfly catheter or extension set may be used to allow the needle to be left in the vein for additional propofol to be titrated to effect. Because of its short duration of effect, it is proposed that propofol is best used in combination with inhalant anesthesia for longer procedures. Propofol has become the author's most popular choice for induction of all reptilian species, including crocodilians, when IV access can be obtained. Even large crocodilians trained to station in a restraint box may be induced with an IV injection with little stress or danger to the animal or handlers.

INHALANT ANESTHESIA

Endotracheal intubation and assisted respiration are recommended for inhalant anesthesia (Schumacher, 1996). Aquatic species are capable of long periods of apnea. Consequently, injectable anesthetics are used for induction to allow safe access for intubation.

Table 18.1. Commonly used drugs in crocodilians.

Drug	Dosage	Species	Remarks	Reference
Analgesia				
Morphine	0.8 mg/kg i.m	C. porosus		Kanui, 1992
Meperidine	1–2 mg/kg i.m.	C. porosus		
Meloxicam	0.1– 0.2 mg/kg			
	IM or PO	Most species		Whiteside, 2004
				Wellehan, 2006
Anesthesia				
Ketamine	11-110 mg/kg IM	Most species	Variable response	Jacobson, 1984
Retailine	11–110 Hig/ kg Hvi	wiost species	when used alone	Frye, 1991
				Millichamp, 1988
				Loveridge, 1972
Ketamine and	10 mg/kg and	Most species		Heaton-Jones, 2002
medetomidine	0.1 mg/kg IM	•		Smith, 1998a
				Smith, 1998b
				Smith, 1998c
Ketamine and xylazine	7.5–10 mg/kg and	Most species		Idowu, 1986
	1–2 mg/kg IM			
Tiletamine/zolazepam	5–15 mg/kg IM	Most species		Jacobson, 1984
Propofol	3–10 mg/kg IV	Most species	Start at low end of	Diver, 1996
Diagonom	0.22.0.62 mg/kg D4	Most species	dose for intubation	Schumacher, 1996
Diazapam	0.22-0.62 mg/kg IM	Most species	Poor IM absorption	Loveridge, 1972
Reversal Agents				
Atipamezole	5 times the dose of	Most species		Heaton-Jones, 2002
тыришедете	medetomidine IM	most species		Smith, 1998a
				Smith, 1998b
				Smith, 1998c
Yohimbine	0.1 mg/kg IM	Most species		Lang, 1987
				Fyre, 1991
Flumazinil	1:13 or 1:20	Most species		Lang, 1987
	times the dose of			Terpin, 1978
NT	benzodiazepine IV	0 "1 "		Jacobson, 1984
Neostigmine	0.03-0.06 mg/kg IM	C. niloticus		Flammard, 1992
				Fleming, 1996
Inhalant Agents				
Isoflurane	1-5%	Most species	2–3% for maintenance	Bennet, 1996
				Schumacher, 1996
Sevoflurane	1-5%		No published use in	Bertelsen, 2005
			crocodilians, but used	Chittick, 2002
TT 1 -1	1.50/		in other reptiles	Rooney, 1999
Halothane	1–5%		Not recommended	Burke, 1996
			owing to hepatotoxicity	
			and cardiotoxicity	
Paralytics				
Gallamine	1–2 mg/kg IM	C. niloticus	NO ANALGESIA	Fleming, 1996
Guillinie	0/0			Frye, 1991
				Jacobson, 1984
				Lang, 1987
				Loveridge, 1979
Succinylcholine	0.33-5 mg/kg IM	Most species	NO ANALGESIA	Blake, 1993
				Jacobson, 1984
				Millichamp, 1988
				Spiegal, 1984

Crocodilians have complete tracheal rings and cuffed endotracheal tubes, if overinflated, may cause avascular necrosis of the tracheal mucosa. To place the endotracheal tube, the snout should be grasped with two hands and the head and neck flexed 90 degrees into a dorsal position. The mandible and maxilla can then be sepa-

rated and a block of wood or other form of speculum. As described, the palatal flap must be displaced to allow visualization of the glottis.

Positive pressure ventilation at a rate of 2 to 4 breaths per minute is adequate for crocodilians (Schumacher, 1996). For crocodilians weighing less than 5 kg a

non-rebreathing system is indicated, with a flow of 300 to 500 ml/kg per minute. For crocodilians greater than 5 kg, a circle system 1 to 2 L/minute for maintenance is recommended (Bennett, 1996). This is lower than in mammals of comparable size, but the oxygen requirements for crocodilians are much lower (Coulson, Hernandez, 1983; Coulson, Herbert, and Coulson, 1989).

Isoflurane provides fast induction, good muscle relaxation, and rapid recovery. Induction is accomplished with 4% to 5% at 2 to 4 L/minute; maintenance rates of 1% to 4% will vary depending on the injectable pre-anesthetic agent used. Recovery should take 10 to 60 minutes, depending on the depth of anesthesia and type of pre-medication agent. Induction and recovery times with halothane are prolonged compared to Isoflurane (Bonath, 1979; Neilson, 1996). The use of sevoflurane has not been described in the literature. However, it has been used in a number of other reptilian species with faster induction and recovery times than isoflurane and minimal cardiopulmonary effects (Rooney et al., 1999; Chittick, 2002; Bertelsen et al., 2005). The popularity of sevoflurane is increasing, and more research with crocodilians is needed.

ANESTHETIC PROTOCOLS

In formulating an anesthetic protocol for a crocodilian it is difficult to provide specific guidelines for each species and situation (Table 18.1). It is important to consider the goal of the immobilization, the species, medical condition, enclosure, temperature, and staffing. Below are a few of the author's suggestions for anesthetizing crocodilians. However, these drugs and doses have not been tested in all crocodilian species and some variability is assumed.

Adults

Medetomidine ($100 \,\mu\text{g/kg}$) and ketamine ($10 \,\text{mg/kg IM}$), intubate, then isoflurane (2--3% in oxygen at $1\text{--}2 \,\text{L/minute}$) via an endotracheal tube (circle system) with forced ventilation at 3 to 4 breaths/minute should be used. When isoflurane equilibrates the medetomidine can be reversed with atipamezole ($500 \,\mu\text{g/kg IM}$).

Gallamine (1–2 mg/kg IM) \pm diazepam (0.25 mg/kg IM). This may be sufficient for non-invasive procedures such as translocation. For invasive procedures (i.e., surgery), maintain with isoflurane in oxygen. The gallamine may be reversed with neostigmine (0.03–0.06 mg/kg IM). Reversal with IV injection is discouraged as the crocodilian may become alert within a few minutes. It is not recommended for use in alligators. Gallamine is no longer commercially available in the United States.

Tiletamine/zolazepam (4–8 mg/kg IM) will be insufficient to reach surgical anesthesia; however, intubation should be possible. Maintain with isoflurane. A long

recovery of 4 to 8 hours may be encountered, and care should be taken not to immerse the crocodilian in deep water during this period.

Juvenile and Restrained Adults

Propofol (3–5 mg/kg IV) (caudal/ventral coccygeal vein). Animals have to be properly restrained or behaviorally conditioned to achieve IV access. Additional propofol may have to be titrated to effect. Maintain with isoflurane in oxygen.

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19 Squamates (Snakes and Lizards)

Mads F. Bertelsen

INTRODUCTION

Sedation and anesthesia in lizards and snakes are used to enable surgery and other painful or invasive procedures, facilitate handling, and enhance the quality or safety of diagnostic procedures while minimizing stress and discomfort. Within the field of reptilian anesthesia there has been a gradual and continuing evolution from hypothermia and manual restraint to balanced, controlled anesthesia. Several excellent reviews on reptile anesthesia are available (Malley, 1997; Bennett, 1998; Heard, 2001), whereas controlled clinical studies are scarce.

TAXONOMY AND BIOLOGY

The nomenclature within the class Reptilia has undergone significant change in the past few years, and taxonomy remains controversial. Briefly, the order Squamata consists of more than 50 families and 7,700 species of lizards and snakes.

ANATOMY AND PHYSIOLOGY

Reptiles are ectothermic vertebrates with relatively low metabolic rates. Their pulmonary and cardiac anatomy, as well as their control of respiration, differs from those of mammals. Despite 200 years of study, many aspects of reptilian anatomy and, more notably, physiology remain poorly understood.

Cardiovascular System

All reptiles possess two atria divided by a complete atrial septum. Each opens into the ventricle by a separate atrioventricular ostium. The ventricle of non-crocodilian reptiles is incompletely divided by a horizontal septumlike muscular ridge. This ridge and an opposing thickening in the ventricular wall divide the ventricle into

two sub-compartments. The incomplete ventricular separation creates the potential for intracardiac mixing or shunting of blood. This may occur as a left to right (L-R) shunt or a right to left (R-L) shunt. A L-R shunt results in oxygenated pulmonary venous blood re-entering pulmonary circulation, whereas a R-L shunt results in a fraction of deoxygenated systemic venous blood bypassing the lungs and returning into systemic circulation, resulting in alveolar to arterial gradients for respiratory gases. The reduction in arterial oxygen pressure in reptiles during R-L shunting is considerable and is well documented in turtles as well as lizards (Hicks and Comeau, 1994; Hlastala et al., 1985; Hopkins, Wang, and Hicks, 1996; Wang and Hicks, 1996).

The extent and direction of shunting is highly dependent on the degree of functional separation, determined by evolutionary adaptations. At one extreme, turtles, which have poorly developed ventricular separation and similar pulmonary and systemic arterial blood pressures, have large intracardiac shunts (Shelton and Burggren, 1976; White, Hicks, and Ishimatsu, 1989; Wang and Hicks, 1996). In contrast, varanid lizards have a very well-developed muscular ventricular septum, and a large difference between pulmonary and systemic pressures (similar to that seen in mammals), resulting in only low-grade shunting (Burggren and Johansen, 1982; Heisler, Neumann, and Maloiy, 1983; Heisler and Glass, 1985). In some species (e.g., varanids) the shunting patterns are essentially identical during apnea and ventilation (Heisler and Glass, 1985). In other species, however, a clear relationship exists between cardiac shunting patterns and the stage of respiration. Breath holding is associated with decreased pulmonary perfusion, and large R-L intracardiac shunts, whereas periods of pulmonary ventilation are characterized by increased pulmonary blood flow leading to a reduction in the R-L shunt (Hicks and Krosniunas, 1996).

Respiratory System

The glottis of most reptiles is located at the base of the tongue, quite rostrally in the oral cavity. It is closed during most of the respiratory cycle, opening only during inspiration and expiration. The squamate trachea has incomplete cartilaginous rings, whereas those of chelonians and crocodilians have complete tracheal rings (Kardong, 1972a,b; Davies, 1981). Lizards and primitive snakes have two roughly symmetrical lungs, whereas in more advanced snakes the left lung is reduced in size or absent. In general, gas exchange occurs in the cranial portion of the lung, whereas the caudal portion may be reduced to an air sac-like structure. The relative lung volume, as well as the compliance of the reptilian lung, far exceeds that of mammals, but the surface available for gas exchange is smaller.

The basic pattern of respiration is an exhalation followed by an inspiration, followed by a nonventilatory period of varying length. Most reptiles exhibit an intermittent breathing pattern characterized by periods of apnea interrupted by brief ventilatory periods consisting of one to several breaths (Templeton and Dawson, 1963; Glass and Wood, 1983; Abe and Johansen, 1987).

Reptiles, most notably freshwater turtles, are remarkably resistant to ambient hypoxia. Although green iguanas can breath hold up to 4 hours (Moberly, 1968), chelonians may survive complete environmental anoxia for hours or days at their normal body temperatures (Belkin, 1963, 1968; Bickler, 1992), and weeks to months at very low temperatures (Ultsch and Jackson, 1982; Hicks and Farrell, 2000). An increase in body temperature leads to increased metabolic oxygen consumption, and consequently to increased ventilation.

Implications for Inhalational Anesthesia

As described, the systemic arterial blood of reptiles may have gas tensions considerably different from the gas within the lung (Hicks and Comeau, 1994; Wang and Hicks, 1996). The main reasons for this gradient are functional intrapulmonary venous admixture and R-L to left intracardiac shunting. Of these two, ventilation/perfusion heterogeneity appears remarkably constant among species, whereas the degree of intracardiac shunting shows marked species differences (Powell and Hopkins, 2004). For example, reported values for the pulmonary to arterial oxygen difference, when breathing 21% oxygen, range from only 13.6 mmHg in monitor lizards (Mitchell, Gleeson, and Bennett, 1981) to 60 to 70 mmHg in turtles (Burggren and Shelton, 1979) and snakes (Seymour and Webster, 1975). In comparison, the pulmonary to arterial difference created by a small physiological shunt in mammals and birds is minor. The consequence is that induction and recovery from inhalational anesthesia may be slower and less predictable than in mammals and birds.

PHYSICAL RESTRAINT

Smaller lizards and snakes are easily restrained by one person, whereas large animals require multiple handlers and possibly the use of boards or catch poles. Very large lizards such as Komodo dragons may be trained or tricked to enter specifically designed restraint boxes, with multiple hatches to allow safe access to various body parts.

Many lizard species show tail autonomy, and may shed a proportion of the tail in response to stress and handling. These species should never be held by the tail alone. All lizards and snakes may bite, and large individuals are capable of inflicting severe bite wounds. Helodermid lizards are venomous and should be handled with extra care, possibly using gloves, snake hooks, or towels (see Chapter 20). Larger lizards may scratch, and some species, particularly varanids, whip inattentive handlers with their tails.

The method of restraint should reflect the size of the animal, defense mechanism of the species, and experience of the handler. Most lizards may be safely restrained by gripping around the neck/shoulder region with one hand and the pelvis with the other. Again, leather gloves and towels may aid in restraint and protect the handler. Short-term restraint for non-painful procedures may be achieved in smaller lizards (including iguanas) by gently pressing on the eyelids from above.

Nonvenomous snakes are restrained by grasping the neck immediately caudal to the head while supporting the body with the other hand. A towel, snake bag, snake hook, or butterfly net may aid in securing the initial grip without getting bitten. In general, an additional handler is required for every meter of snake. For restraint and handling of venomous snakes, see Chapter 20.

VASCULAR ACCESS SITES

The most reliable vascular access site is the ventral tail vessels, located immediately ventral to the coccygeal vertebrae. In snakes, these vessels are usually approached from the ventral midline, but in lizards a lateral approach is often more convenient. The palatine veins may be accessed in larger anesthetized snakes (Figure 19.1). Indwelling catheters may be placed in the cephalic, femoral, abdominal, or ventral cervical vessels using cut-down techniques. Fluids and certain drugs may be administered by the intraosseous route. In lizards, intraosseous catheterization may be performed in the humerus, femur, or tibia following local analgesia of the cannulation site. In snakes cardiac puncture has been used for drug administration as well as for obtaining blood samples. However, the procedure is likely stressful and this approach can not be recommended as damage to the myocardium may occur.



Figure 19.1. The oral cavity of an anesthetized amelanistic Burmese python (Python molurus bivittatus) showing placement of a palatine vein catheter for fluid and drug administration. (Photograph courtesy of Dr Darryl Heard.)

PREANESTHETIC CONSIDERATIONS

Body weights vary markedly, and an accurate weight should be obtained prior to drug administration. The hydration status of the subject should also be assessed and abnormalities corrected. Animals should be subjected to a physical examination prior to anesthesia; and if time, budget, and facilities allow, a blood sample for PCV, CBC, and plasma biochemistry profile, as well as ultrasonographic or radiographic imaging may aid in pre-anesthetic evaluation. Starving the animals prior to surgery is not generally indicated, but in carnivorous species, large prey items in the stomach may theoretically impair pulmonary function.

MAINTAINING BODY TEMPERATURE

Induction time, anesthetic dose, and recovery time (Green et al., 1981; Arena, Richardson, and Cullen, 1988; Dohm and Brunson, 1998), as well as general metabolism, are all temperature dependent; maintaining the animalís body temperature within the preferred optimum zone is crucial. This is achieved through the use of heating pads, circulating water blankets, water bottles, bean bags, etc. For most temperate and tropical species, a body temperature of 25° to 35°C during induction, anesthesia, and recovery is appropriate.

MONITORING

Physiological Function

Most monitoring modalities known from domestic species may be applied to reptiles. Body temperature should be monitored with a cloacal thermometer or temperature probe able to measure low temperatures. Heart rate and rhythm may be monitored using electrocardiography or Doppler flow detection units. In snakes, the heart rate usually may be determined by visual inspection of the ventral scales approximately 25% of the snakeís length from the head. Respiration may be assessed visually, and mainstream or sidestream capnography provides useful information in intubated animals.

The use of pulse oximetry in reptiles remains controversial (Diethelm et al., 1998; Mosley, Dyson, and Smith, 2004) as values obtained may not correlate with measured arterial oxygenation and calculated saturations (Mosley, Dyson, and Smith, 2004).

Arterial blood gas analysis can provide valuable information on oxygenation and acid-base status. Although cost-effective portable equipment is increasingly available, the difficulty of obtaining arterial blood samples reduces relevance in the clinical setting. Venous blood samples are readily available and may partly reflect arterial values. In anesthetized iguanas, for example, arterial and venous oxygen pressures may be almost identical, and carbon dioxide pressure only slightly different, which may suggest very low tissue metabolism and oxygen consumption during anesthesia (Mosley, Dyson, and Smith, 2004).

Depth of Anesthesia

The clinical signs associated with induction of general anesthesia in reptiles are fairly consistent. Generally, muscle relaxation in lizards starts at mid-body and moves forward, then backward so that tail tone is lost last (Bonath, 1977; Bonath and Zschege, 1979). In varanids induced with inhalation anesthetics, the front limbs lose tone first, followed by the hind limbs and neck approximately simultaneously. Then righting reflex is lost, and finally the tail tone (Bertelsen et al., 2005b). This sequence does not appear to be dependent on the anesthetic regimen used. The tongue retraction reflex in snakes and varanids persists beyond the loss of tail tone and righting reflex (Schumacher et al., 1997), and often is present at the surgical plane, as is the corneal reflex (Arena, Richardson, and Cullen, 1988). Loss of these reflexes may indicate excessive anesthetic depth. Animals retain the ability to react to painful stimuli even after the loss of righting reflex and tail tone, and the response to toe or tail pinching should be evaluated before deciding that surgical anesthesia has been achieved.

ENDOTRACHEAL INTUBATION

Because of the large oral cavities and rostral position of the glottis, lizards and snakes are easily intubated. The glottis is visualized at the bottom of the mouth, immediately caudal to the tongue (Figures 19.2A and B). A non-cuffed endotracheal tube of appropriate size is inserted and taped in place, allowing positive pressure





Figure 19.2. A. The oral cavity of a boa constrictor (Boa constrictor). Note the rostral location of the partly open glottis. **B.** The oral cavity of a boa constrictor showing the endotracheal tube within the glottis after intubation.

ventilation, either manually or using mechanical ventilators. Snakes and some lizards may be intubated awake, following the application of topical analgesics to the glottis. Endotracheal tubes are commercially available down to 1 mm ID. Over-the-needle IV catheters (16–19 G) may be used for the smallest reptiles.

A piece of rubber tubing, a folded gauze pad or wooden mouth gag, depending on the size of the subject, may be used to prevent the animal from biting the tube. In small reptiles, taping the animal, endotracheal tube, and breathing system to the table or a tongue depressor may prevent tube displacement and injury.

VENTILATION

The combination of very low metabolic rates and extreme resilience to hypoxemia allow anesthetized reptiles to experience long periods of apnea without deleterious effects. However, until more is known about the exact requirements, mechanical ventilation is recommended during deep or prolonged anesthesia. Apart from preventing hypoxemia, mechanical ventilation ensures delivery and removal of inhalational anesthetic agents.

Following endotracheal intubation, mechanical ventilation may be achieved by manually "bagging" the animal or by means of a ventilator of appropriate size. For many species specialized laboratory animal or very small animal equipment is necessary to avoid overventilation, and even with this equipment it may be hard to achieve respiratory rates that are low enough. When artificially ventilating lizards and snakes, the larger tidal volume and lower minute ventilation compared with mammals should be taken into consideration, and if available, capnography should be used to monitor the level of ventilation. A minute ventilation of 50 to 75 ml/kg and a frequency of 1 to 4 breaths/minute is adequate in most species.

INHALATIONAL ANESTHESIA

Inhalation agents are commonly used for induction and maintenance of reptile anesthesia (Read, 2004). As in other species, the advantages of inhalation anesthetics include superior control of depth, wide safety margins, excellent muscle relaxation, faster recovery, and "built-in" oxygen supplementation. As mentioned, induction and recovery times in reptiles tend to be longer and more variable than in mammals and birds, because of breath holding, intracardiac shunting, and slow circulatory time.

Anesthetic Potency

Minimum alveolar concentration or minimum anesthetic concentration (MAC) is the standard measure of potency of inhalational anesthetic agents (Quasha, Eger, and Tinker, 1980). MAC is defined as the anesthetic concentration that prevents gross purposeful movement in 50% of an anesthetized population subjected to a supramaximal noxious stimulus, traditionally a surgical incision. Apart from permitting comparison of anesthetic agent potency, the value allows standardization and comparison of various depths of anesthesia as multiples of MAC. Using MAC values also provides a way of assessing the synergism between two anesthetics. Other terms, essentially equivalent to MAC are sometimes reported in birds and reptiles (e.g., minimum anesthetic dose, effective dose 50, minimum infundibular concentration). Generally, MAC for a given agent varies little across mammalian species (Quasha, Eger, and Tinker, 1980) and the limited number of reports available indicate that the same applies to reptiles, although evolutionary differences in cardiopulmonary performance may give rise to greater variability among reptiles (Bertelsen et al., 2005c). As MAC only accounts for 50% of the population, vaporizer settings of 1.3 MAC are recommended to achieve surgical anesthesia.

Equipment

Inhalant anesthetics are delivered by agent-specific vaporizers using oxygen or a mix of oxygen and nitrous oxide as the carrier gas. Standard anesthetic machines fitted with non-rebreathing (Bain's) or circular systems are used, and for smaller specimens laboratory animal equipment (e.g., Anesthesia Work Station, Halowell EMC, Pittsfield, MA) has great potential. Commercially available small animal face masks, as well as masks made from plastic bottles or syringe cases work well.

Oxygen consumption is low (less than 1 ml/kg per minute) because of low metabolic rates (Perry, 1989) and flow rates may be reduced considerably compared with mammalian settings. In practice, the flow rate is often determined by the performance of flow meters and vaporizers and rates of 250 to 1,000 ml/minute are appropriate for most reptiles.

Although reptiles can down-regulate respiration in response to hyperoxemia (Glass and Johansen, 1976), delivery of inhalants in room air (21% oxygen) does not appear to result in higher respiratory rates and faster inductions than in 100% oxygen (Bertelsen et al., 2005b).

INHALATIONAL ANESTHETICS

Early Inhalants

One of the first reports of anesthesia in reptiles is that of John Tait, who described the surgical removal of venom glands from rattlesnakes under chloroform anesthesia (Tait, 1938). Later, prolonged induction and recovery periods were described in several snake species anesthetized with methoxyflurane (Gandal, 1966; Burke and Wall, 1970). There are no recent reports on the use of either agent, and the drugs have long been superseded by newer agents.

Ether anesthesia is associated with very long induction (40–60 minutes) and recovery periods in lizards and snakes (Brazenor and Kaye, 1953; Bonath and Zschege, 1979). Although still occasionally used in physiological research and venom production, ether must be considered obsolete in a clinical setting. It is also flammable and explosive and, therefore, a hazardous chemical to store and use.

Halothane

Halothane (3%–6%) results in moderate sedation to profound anesthesia. At high halothane concentrations (5.8%) the mean induction time at 22°C to 25°C was

24 minutes in lizards (n = 38), and 35.3 minutes in snakes (n = 12) (Bonath, 1977, 1979; Bonath and Zschege, 1979). Shorter induction times (5–19 minutes) were reported using halothane (5%) in a 3:1 nitrous oxide/oxygen mixture (Custer and Bush, 1980).

A transient initial excitement stage has been described in rattlesnakes at very high doses (Hackenbrock and Finster, 1963). In snakes, halothane significantly decreases respiration rate and tidal volume (Bonath, 1977, 1979; Bonath and Zschege, 1979; Custer and Bush, 1980), leading to respiratory acidemia (Custer and Bush, 1980), whereas heart rate decreases mildly or remains unchanged (Bonath, 1977, 1979; Bonath and Zschege, 1979; Custer and Bush, 1980).

Recovery times following brief anesthetic events are relatively short (24–35 minutes), whereas recovery times from deeper anesthesia are much longer (Bonath, 1977, 1979; Bonath and Zschege, 1979).

No information exists on the potency of halothane in reptiles, and data on cardiopulmonary function during halothane anesthesia is limited to that described in the preceding. Halothane continues to be used in physiological research, but clinically has been replaced by isoflurane and sevoflurane.

Isoflurane

Unlike chelonians in which inductions may be prohibitively prolonged, mask induction is feasible in lizards (Figure 19.3) and snakes. In lizards, the time to initial relaxation and loss of righting reflex is typically 4 to 9 minutes (Schildger et al., 1993; Spelman et al., 1996; Hernandez-Divers et al., 2005), whereas the time to complete relaxation is 13 to 20 minutes, depending on



Figure 19.3. Mask induction of a monitor lizard with isoflurane. Note the use of a standard small animal face mask.

the species (Mosley, 2000; Bertelsen et al., 2005b). In snakes, induction times with mask induction tend to be slightly longer (Schildger et al., 1993), but direct intubation of the awake snake followed by mechanical ventilation with the drug leads to rapid induction. At low levels animals continue breathing, but at levels adequate for surgical anesthesia mechanical ventilation is usually necessary.

Isoflurane causes a moderate (25%) reduction in heart rate (Maas and Brunson, 2002; Hernandez-Divers et al., 2005) and a severe reduction in respiratory rate (Maas and Brunson, 2002) compared with values in manually restrained animals. It should be considered, however, that values in manually restrained subjects are significantly higher than in undisturbed animals (Bertelsen et al., 2005b). During anesthesia, a dosedependent reduction in systemic blood pressure and heart rate is observed (Mosley, Dyson, and Smith, 2004).

The MAC at 30°C to 32°C has been reported to be $1.9 \pm 0.59\%$ in rat snakes (Maas and Brunson, 2002), $2.1 \pm 0.6\%$ in iguanas (Mosley, Dyson, and Smith, 2003a), and $1.54 \pm 0.17\%$ in monitors (Bertelsen et al., 2005c). These numbers indicate that vaporizer settings of 2% to 2.5% are appropriate to maintain surgical anesthesia in most subjects. MAC decreases with decreasing body temperature (Dohm and Brunson, 1998). In an attempt to determine the cardiac anesthetic index, seven iguanas were subjected to up to 9.2% isoflurane without any apparent signs of cardiac arrest, suggesting a very wide margin of safety (Mosley, Dyson, and Smith, 2003b).

Recovery time depends on the depth and duration of anesthesia, and is relatively short (2–12 minutes) following brief, shallow anesthetic events (Schildger et al., 1993; Spelman et al., 1996), intermediate (30–40 minutes) following light surgical anesthesia, and more prolonged (50–70 minutes) following deep anesthesia (Mosley, 2000; Bertelsen et al., 2005b). In general, recovery times appear longer and more variable in snakes than lizards.

Sevoflurane

Induction times using sevoflurane are slightly shorter than with isoflurane (Hernandez-Divers et al., 2005; Bertelsen et al., 2005b). In lizards, the time to initial relaxation and loss of righting reflex is around 6 minutes (Hernandez-Divers et al., 2005), whereas the time to complete relaxation is approximately 11 minutes (Bertelsen et al., 2005b). As for isoflurane, direct intubation of the awake animal followed by mechanical ventilation with the drug leads to rapid induction. The addition of 66% nitrous oxide will speed up inductions slightly (Bertelsen et al., 2005b).

Sevoflurane induction has been subjectively judged as smoother and associated with less breath holding than with isoflurane (Hernandez-Divers et al., 2005), but the respiratory rate during induction appears to be

similar or even marginally lower with sevoflurane (Bertelsen et al., 2005b). Sevoflurane causes a moderate reduction in heart rate (Maas and Brunson, 2002; Hernandez-Divers et al., 2005) and a severe reduction in respiratory rate (Maas and Brunson, 2002) compared with values in manually restrained animals. No detailed data on the dose-related hemodynamic effects of sevoflurane in snakes and lizards have been published, but responses appear to be similar to those with isoflurane.

The MAC at 30°C to 32°C has been reported to be $2.42 \pm 0.57\%$ in ratsnakes (Maas and Brunson, 2002) and $2.51 \pm 0.46\%$ in monitor lizards (Bertelsen et al., 2005a), indicating that vaporizer settings of around 3% are appropriate to maintain surgical anesthesia. In a recent study, the co-administration of 66% nitrous oxide resulted in a 26% reduction in sevoflurane MAC (Bertelsen et al., 2005a), and similar reductions are likely to occur in other species and with other inhalants.

With the modern inhalant anesthetics, the length of the recovery period appears to be influenced more by the duration and depth of anesthesia than by the agent used. After a short administration time, sevoflurane will result in faster recoveries than isoflurane (Hernandez-Divers et al., 2005), but following prolonged, deep anesthesia that difference is marginal (Bertelsen et al., 2005b).

Nitrous Oxide

Nitrous oxide (N_2O) may be used as a supplemental anesthetic (at 50%–66% with oxygen) during induction with inhalational agents (Custer and Bush, 1980; Bennett et al., 1999) resulting in marginally shorter induction times (Bertelsen et al., 2005b). In monitors, 66% N_2O delivered with sevoflurane reduced the sevoflurane requirement (MAC) 25% (Bertelsen et al., 2005a). Assuming that a relationship of simple linear additivity between sevoflurane and nitrous oxide exists, the MAC for N_2O in varanid lizards can be estimated to be 244%. Apart from reducing the concentration of the primary agent, which may improve cardiopulmonary function, the use of N_2O likely provides improved analgesia over delivery in 100% oxygen.

Carbon Dioxide

Carbon dioxide (CO₂) is occasionally used for the immobilization of venomous snakes during venom extraction (Wang, Fernandes, and Abe, 1993). Unconsciousness is thought to be mediated through central nervous system acidosis, and this procedure is not recommended in clinical practice.

A mixture of 3% to 5% $\rm CO_2$ in oxygen may be used during mechanical ventilation to achieve high oxygenation and delivery of inhalational agents while avoiding the respiratory acidemia seen during hyperventilation (T. Wang, personal communication), and the use of a 10% $\rm CO_2$ mixture has been suggested to stimulate respiration during recovery (Malley, 1997).

PARENTERAL ANESTHESIA

Numerous injectable anesthetics have been used in snakes and lizards with varying success. These include etorphine hydrochloride (Hinsch and Gandal, 1969; Wallach and Hoessle, 1970), pentobarbital sodium (Karlstrom and Cook, 1955; Betz, 1962; Arena, Richardson, and Cullen, 1988), thiopental sodium (Karlstrom and Cook, 1955), methohexital (Wang, Kubie, and Halperm, 1977), MS-222 (Karlstrom and Cook, 1955; Green and Precious, 1978), urethane (Calderwood, 1971), nicotine (Calderwood, 1971), decamethonium iodide (Brazenor and Kaye, 1953), tubocurarine chloride (Brazenor and Kaye, 1953), procaine hydrochloride (Livezey, 1957), and alphaxalone/alphadolone (Calderwood and Jacobson, 1979; Lawrence and Jackson, 1983). With the possible exception of alphaxalone/alphadolone, these agents must be considered obsolete in clinical practice. Of the remaining agents, propofol is the agent of choice provided that vascular access can be gained in the awake animal.

Propofol

Propofol (5–10 mg/kg IV or IO) causes induction in 1 to 5 minutes (Bennett et al., 1998; Anderson et al., 1999). Propofol administered perivascularly is ineffective, but unlike barbiturates does not cause tissue damage. Administration via the ventral tail vessels is generally feasible in patients larger than 250 g, although there are significant species differences.

In lizards and snakes, propofol causes a slight decrease in heart rate and a marked respiratory depression (Bennett et al., 1998; Anderson et al., 1999). The respiratory depression is dosage dependent and appears to be affected by the duration of administration. Low doses given slowly cause less apnea than high doses administered as a bolus.

The duration of anesthesia depends on the dosage. Low dosages (e.g., 5 mg/kg) result in 20 to 30 minutes of anesthesia while longer recovery times are seen following high dosages (e.g., 10 mg/kg). Anesthesia may be maintained by inhalation or by continuous propofol infusion. An infusion rate of 0.5 mg/kg per minute proved excessive in green iguanas (Bennett et al., 1998), and rates of 0.2 to 0.4 mg/kg per minute are likely more appropriate. For most species a dosage of 5 to 8 mg/kg given slowly is appropriate for short procedures or as induction for inhalational anesthesia. High cost and short shelf-life once vials are open have been listed as disadvantages (Bennett, 1998), but in the author's experience, propofol transferred to sterile Vacutainer vials and stored upright and refrigerated retains its effect and may be used without deleterious effects for at least 6 months.

Ketamine

Ketamine hydrochloride has been used extensively in reptiles, primarily snakes, since its discovery in the late 1960s (Glenn, Straight, and Snyder, 1972; Schumacher et al., 1997). The effective dosage depends on the body temperature (Arena, Richardson, and Cullen, 1988); at lower body temperatures lower dosages are required, but longer induction and recovery times are observed (Green et al., 1981; Arena, Richardson, and Cullen, 1988). Effects are highly species dependent (Cooper, 1974; Ogunranti, 1987; Arena, Richardson, and Cullen, 1988; Schildger et al., 1993; Hill and Macklessy, 1997), but large individual variation is also observed (Cooper, 1974; Hill and Macklessy, 1997).

Recommended dosages range from 12 to 44 mg/kg for sedation (Glenn, Straight, and Snyder, 1972; Schildger et al., 1993; Spelman et al., 1996; Bennett, 1998) to 55 to 88 mg/kg for surgical anesthesia (Glenn, Straight, and Snyder, 1972; Schildger et al., 1993; Bennett, 1998), whereas yet higher doses (100–220 mg/ml) are reported occasionally (Harding, 1977; Arena, Richardson, and Cullen, 1988). The time to peak effect following intramuscular injection is approximately 30 minutes (Glenn, Straight, and Snyder, 1972; Cooper, 1974; Custer and Bush, 1980; Green et al., 1981).

In snakes and lizards, moderate ketamine dosages are associated with increased heart rates (Arena, Richardson, and Cullen, 1988; Schumacher et al., 1997), hypertension (Schumacher et al., 1997), and respiratory depression (Ogunranti, 1987; Arena, Richardson, and Cullen, 1988; Schumacher et al., 1997), the latter peaking at 30 to 60 minutes (Ogunranti, 1987; Arena, Richardson, and Cullen, 1988). At increasing dosages the drug will induce apnea, bradycardia (Glenn, Straight, and Snyder, 1972; Cooper, 1974; Custer and Bush, 1980; Green et al., 1981) and eventually death.

The main disadvantage of using ketamine in reptiles is extended recovery periods. Time to complete recovery depends on dosage and may approach 7 days at very high dosages (Glenn, Straight, and Snyder, 1972). Reported recovery times range from 6 to 24 hours at 15 mg/kg (Hill and Macklessy, 1997) to 2 to 3 days at 40 to 80 mg/kg (Glenn et al., 1972; Custer and Bush, 1980; Green et al., 1981) and 6 to 7 days at 100 to 130 mg/kg (Glenn, Straight, and Snyder, 1972).

Ketamine may be combined with sedatives such as benzodiazepines and α_2 -agonists for better muscle relaxation and a reduction in required dose (Malley, 1997; Bennett, 1998; Heard, 2001). Because of the variable effects, long recovery periods and the availability of alternative protocols the author rarely uses the dissociative agents.

Zolazepam-Tiletamine

The potent cycloheximide tiletamine combined with the benzodiazepine zolazepam has found some use in reptile anesthesia (Bush and Beck, 1974; Boever and Caputo, 1982; Read, 2004), but very little published information exists. The onset of effects is faster than with ketamine (Mauthe von Degerfeld, 2004), whereas cardiopulmonary effects are likely similar to those

produced by ketamine. In early studies, dosages of 30 to 40 mg/kg administered to iguanas resulted in surgical anesthesia lasting 8 to 16 hours, whereas variable effects were seen with dosages of up to 88 mg/kg in snakes (Boever and Caputo, 1982). In Komodo dragons dosages of 5.5 mg/kg caused repetitive head and neck movements 10 to 25 minutes before resulting in sedation (Spelman et al., 1996). In iguanas zolazepam/tiletamine (10 mg/kg) resulted in a brief period of excitement followed by good relaxation (Mauthe von Degerfeld, 2004). Despite its long duration of action and variable effects, low doses (2–5 mg/kg) may be useful for sedation prior to handling or intubation, particularly of larger animals.

Sedatives

Sedative and tranquilizing drugs such as benzodiazepines and α_2 -agonists may be used in squamates, but studies to document their effects are lacking. Because of the difficulty in accessing the vascular system and airways in chelonians there has been much more focus on the use of these drugs in turtles and tortoises, and as results may likely be extrapolated to snakes and lizards, readers are referred to Chapter 21.

OTHER TECHNIQUES

Hypothermia, once used as a means of immobilizing reptiles (Kaplan, 1969; Calderwood, 1971) is considered an unacceptable clinical practice, as is electroanesthesia (Northway, 1968).

RECOVERY

As mentioned, recovery times in reptiles are prolonged compared with birds and mammals. Body temperature critically affects speed and quality of recovery, so animals should be kept warm. If mechanical ventilation was used, this should be continued until animals are able to breathe unassisted. Periods of apnea of 5 to 10 minutes, however, are unlikely to cause deleterious effects.

Since hyperoxemia may down-regulate respiration in reptiles (Glass and Johansen, 1976), recovery in room air (21% oxygen) as opposed to 100% oxygen has been suggested (Diethelm and Mader, 1999). However, although faster recoveries were experienced when ventilating iguanas with 21% oxygen following short time isoflurane anesthesia (Diethelm and Mader, 1999), no difference could be demonstrated following longer anesthetic events (Bertelsen et al., 2005b).

COMPLICATIONS

Complications are relatively rare using the protocols suggested, but respiratory depression or apnea and prolonged recoveries are among those most commonly encountered (Read, 2004). These problems may be reduced by providing adequate mechanical ventilation and by maintaining body temperature within physiological limits.

ANALGESIA

Disappointingly little work has been done pertaining to pain perception and modulation in reptiles (Machin, 2001). In the green iguana, butorphanol (1 mg/kg IM) failed to decrease the minimum anesthetic dose of isoflurane (Mosley et al., 2003a), and did not provide demonstrable analgesia in a heat pad test (Robinson and Fleming, 2005). Butorphanol (2 mg/kg IM) administered to iguanas caused minimal sedation and did not result in significant changes of heart and respiratory rates (Hernandez-Divers et al., 2005). Even at doses up to 28 mg/kg butorphanol did not alter thermal withdrawl latency (Sladky et al., 2006). However in anoles, the administration of morphine (5 mg/kg IM) caused a latency of the tail flick response (Mauk et al., 1981). In red-eared sliders hindlimb withdraw latency was significantly increased with morphine (1.5 mg/kg & 6.5 mg/kg, SC) (Sladky et al., 2006). Despite the lack of documented effects, analgesics should be part of any anesthetic regimen that involves potentially painful procedures. Opioids (e.g., butorphanol) and nonsteroidal anti-inflammatory drugs (e.g., meloxicam and flunixin) are the most commonly used agents (Read, 2004), and until further research becomes available dosages must be extrapolated based on data from other species. It does appear, however, that although butorphanol is the most widely used opioid morphine may be a more appropriate choice, possibly due to a predominance of μ receptors in reptiles. As in any species, preemptive analgesia offers intraoperative as well as postoperative analgesia, and likely will reduce the amount of anesthetic needed. Local analgesics (e.g., lidocaine) are commonly used in reptiles. In small subjects, diluting the drugs prior to administration will help to avoid overdosing.

SELECTED PROTOCOLS

For most snakes and lizards the author recommends one of three approaches (Table 19.1): induction with propofol followed by isoflurane or sevoflurane anesthesia for longer duration; direct intubation and induction with isoflurane or sevoflurane; mask (Figure 19.3) or chamber induction with isoflurane or sevoflurane. For large and aggressive specimens, injection with low doses of ketamine or tiletamine/zolazepam, with or without medetomidine or midazolam, may be used to allow safe handling. Dosages of commonly used drugs are presented in Table 19.2.

Table 19.1. Recommended anesthetic protocols for squamates (snakes and lizards).

Reptile	Pre-medication	Induction	Maintenance	
Snakes, small	None	Propofol 5–10 mg/kg IV Direct intubation ^a followed by	Isoflurane or sevoflurane by endotracheal tube	
		ventilation with isoflurane or	chaothereal tabe	
		sevoflurane		
		Mask with isoflurane or sevoflurane		
Snakes, large	Zolazepam/tiletamine (5–10 mg/kg IM) or None	Propofol 2–7 mg/kg IV	Isoflurane or sevoflurane by	
		Direct intubation ^a followed by ventilation with isoflurane or sevoflurane	endotracheal tube	
Snakes, venomous	None	Propofol 5–10 mg/kg IV ^b	Isoflurane or sevoflurane by endotracheal tube	
		Chamber-induction with isoflurane or sevoflurane		
Lizards, small	None	Propofol 5–10 mg/kg IV	Isoflurane or sevoflurane by	
		Chamber-induction with isoflurane or sevoflurane	endotracheal tube	
Lizards, large	Zolazepam/tiletamine	Propofol 5–10 mg/kg IV	Isoflurane or sevoflurane by	
. 0	(5–10 mg/kg) or None	Mask with isoflurane or sevoflurane	endotracheal tube	

^aDesensitization of the glottis with a drop or spray of local analgesic is recommended.

Table 19.2. Selected anesthetic and analgesic drugs used in squamates (snakes and lizards).

Generic Name	Dosage (mg/kg)	Reversal Agent	Source
Propofol	3–10	None	Bennett et al., 1998; Anderson et al., 1999
Midazolam	1-2	Flumazenil	,
Medetomidine	0.05-0.15	Atipamezole	
Ketamine	10–40 ^a	None	Glenn et al., 1972; Custer and Bush 1980; Schumacher et al., 1997
Zolazepam-tiletamine	2–10	Flumazenil for zolazepam	Mauthe von Degerfeld, 2004
	MAC (%)		
Isoflurane	1.5–2.1		Maas and Brunson. 2002; Mosley et al., 2003a; Bertelsen et al., 2005c
Sevoflurane	2.5		Maas and Brunson, 2002; Bertelsen et al., 2005a
Nitrous oxide	220		Bertelsen et al., 2005a

^aDosages up to 220 mg/kg have been reported (Arena et al., 1988).

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20 Venomous Reptile Restraint and Handling

Frederick B. Antonio

INTRODUCTION

This chapter presents information and recommendations for the restraint of venomous reptiles in either a clinical environment or field conditions. For simplicity, a venomous reptile refers to venomous snakes. A section at the end of the chapter reviews management of venomous lizards of the family Helodermatidae (Gila monsters and beaded lizards). Envenomation is referred to as snakebite, although it is recognized that helodermids can also inflict a serious bite. It is intended that employment of the techniques described in this chapter will greatly reduce the probability of snakebite.

In recent years captive venomous reptiles have increased in popularity. They are the topics of numerous television series, and are portrayed as both exciting and dangerous, often by actors and commentators who inspire young viewers to engage in interactions with venomous species. Many private collectors, researchers, and zoo professionals have only a vague notion of the potential lethality of their charges. The ignorance includes both the potential physiological effects of venoms and behaviors that make venomous snakes difficult to restrain (Altimari, 1998). Some states within the United States prohibit personal possession of venomous reptiles, whereas others lack any regulation. Florida issues over 500 personal possession venomous reptile permits annually. Many private collections are "underground" and reptile clinicians should expect to examine virtually any species of native or exotic venomous reptile. Safe handling of these animals requires that veterinarians, researchers, and support staff must be familiar with and use proper methodologies. The following presents current procedures and techniques to limit unrestrained contact with venomous reptiles and thereby promote safety during examinations, clinical procedures, and field work.

General Characteristics

Snake venoms evolved primarily to aid in prey acquisition and secondarily for defense. More than 2,700 snake

species are currently recognized within about 18 families and 420 genera (Greene, 1997). Of these, 250 to 500 species may induce serious physiological effects in humans. These belong primarily to the families Elapidae (cobras, kraits, mambas, coral snakes, and seasnakes) and Viperidae (true vipers and pitvipers).

Almost every colubrid snake family has at least one species whose venom has the potential to produce either morbidity or mortality in humans. These include (Fry, 2006) Colubridae (Dispholidus, Thelatornis), Dipsadidae (Hydrodynastes, Xenodon, Waglerophis), Atractaspididae (Atractapis, Homoroselaps), Homalopsidae (Cerberus, Enydris, Homalopsis), Natricidae (Macropisthodon, Rhabdophis), Psammophiidae (Malpolon, Psammophis, Rhamphiophis), and Pseudoxyrhophiidae (Leioheterodon, Madagascarophis). Of these, the most commonly imported are the boomslang, Dispholidus typus; African twigsnake, Thelotornis capensis; Blanding's treesnake, Boiga blandingi; road guarder, Conophis lineatus; Japanese water snake, Rhabdophis tigrinus; and the false pitvipers, Xenodon spp.

In a recent study (Fry et al., 2006) of the evolution of reptilian venom systems, additional "non-venomous" snake taxa and some lizards of Varanidae (monitor lizards) and Iguania were added to those known to have toxin-secreting oral glands. Studies of this kind confirm toxic salivary secretions in extant reptiles, usually products of the Duvernoy's gland, present a continuum of toxins whose presence and effect require further study to evaluate their effect in humans. Thus, it is prudent for the clinician to treat suspect or unusual species, especially opisthoglyphs, with the same precautions as recognized venomous species.

Venom delivery systems originate from modified salivary glands. These vary from mucous producing oral glands to well-developed encapsulated glands with separate compressor musculature to express venom through a duct to individual hollow fangs. There are four dental patterns in snakes (Greene, 1997): aglyphous, undifferentiated maxillary teeth, present in primitive snakes



Figure 20.1. Full face shields and protective garments are recommended when working with all species of spitting cobras. (Red spitting cobra, Naja pallida, Central Florida Zoological Park.)

and some colubrids; opisthoglyphous, enlarged teeth (may be grooved to facilitate induction of salivary secretions) located on the posterior ends of the maxillary bones, present in rear-fanged snakes; proteroglyphous, enlarged true hollow fangs located on the anterior end of the maxillary bones that have restricted movement, present in elapids; and solenoglyphous, elongated hollow fangs located on highly movable maxillary bones, fangs are folded back along the roof of the mouth when not in use, present in vipers and pitvipers. These four basic dental morphologies represent a progression in capability of salivary or venom induction when biting.

One impressive variation in fang structure with management implications is found in the elapid species referred to as spitting cobras (Hemachatus haemachatus, Naja nigricollis, Naja mossambica, Naja pallida, and some subspecies of Asian Naja naja). These species have a fang structure and discharge orifice to defensively eject venom at the eyes of an intruder. Target accuracy and the distance of ejection are from 1 to 5 meters (Russell, 1980). Full face shields (Figure 20.1) are recommended at all times when working these species. If venom comes in contact with an eye, wipe remaining venom away from the eyes and begin immediate copious irrigation with sterile saline solution (Boyer and Murphy, 1999). A long-sleeved lab coat or protective garment is recommended to shield skin. Venom may also be expressed on the inside of a restraint tube. Expelled venom must be treated with extreme caution during both the procedure and the clean-up process. Dried venom on glass can be aerosolized during cleaning and cause injury to eyes and mucous membranes.

SNAKE BEHAVIOR

Handling and restraint are approached every time as novel experiences that may be significantly different from the previous ones. Planning the procedure with the total focus of all persons involved is required. Complacency or a casual approach, no matter how experienced the handler, can result in an unexpected and disastrous outcome.

Every species exhibits different behaviors when manipulated. Defensive behaviors vary with individual temperament and the handler must observe and read these behaviors to adjust response and technique. Altimari (1998) describes the temperaments of many captive venomous snake species. Viperids tend to defensively coil and may strike in any direction. Elapids are more dangerous to manipulate and may initially attempt to flee. However, they can turn and strike at any time, or strike first then look for an escape route. Striking distances are approximately two-thirds of the total body length. However, for some species when traveling and lunging while striking it is difficult to determine a safe working distance in an open environment. Always overestimate the strike range.

Snakebite

In the United States prior to 1950, exotic venomous snakes were primarily found in zoos. Increased interest in reptiles during the latter twentieth century has resulted in the United States being the major importer of reptiles, representing 80% of the world trade or approximately 2 million importations annually (Keyler, 2006). The vast majority of snakebites occur in private collections, comprising a large variety of genera and species (Seifert, 2006a). Of these nearly half are elapid bites. The incidence of non-native envenomations has increased significantly over the past 4 years. Statistics on snakebite in clinical situations are difficult to obtain, as many are not reported to data surveillance systems. Toxic Exposure Surveillance System (TESS) data for 2002 showed the number of exotic snakebites in the United States to be 125 (Keyler, 2006).

In a survey of 40 academic institutions that used venomous reptiles in research projects (Ivanyi and Altimari, 2004) 18 facilities reported 42 envenomations and six dry bites from 20 species. The majority of these bites (87.5%) were the result of inappropriate capture techniques and inadequate restraint methods, including free handling snakes, pinning, handling with gloves, and improper use of restraint tubes. Card and Roberts (1996) surveyed North American zoos to determine the incidence of venomous reptile bites received by staff. Out of 30 reptile collections that maintained venomous reptiles, 21 zoos reported a staff member bitten during a 25-year period with a total of 31 incidents. Of these, 15 envenomations occurred during routine handling, five during physical restraint, and one during a veterinary procedure. In a survey of 32 venom extraction facilities worldwide (Powell, Sánchez, and Pérez, 2006) envenomation averaged one per facility every 2 years. Although records of envenomation in veterinary medicine are lacking, the potential is ever-present when a client presents a venomous reptile for examination and treatment. In many cases this is a novel experience for the practitioner who lacks behavioral knowledge of the species, handling expertise, and proper equipment.

Antivenom

Antivenom is the only product recommended for treatment of snakebite. The goal of this immunotherapy is to neutralize venom components with antibodies and prevent them from reaching their sites of action. All snakebites are medical emergencies requiring effective response protocols and knowledgeable case approach by the treating physicians. Treatment of snakebite is outside the scope of this chapter, but it remains the responsibility of the veterinary clinician or researcher to either possess the appropriate antivenom or know the nearest local source for the species to be restrained.

The appropriate foreign antivenom for exotic snakes should be present when working with these species. It should be provided by the client and accompany the snake during transport. Antivenom for native species is usually stocked at local hospitals for regional snake species. It is recommended to contact local hospital pharmacies to periodically check current inventories because antivenom can be difficult to obtain and supplies may be limited.

Treatment of envenomations is a challenge to U.S. physicians; most have never treated a snakebite victim. Case approaches, the appropriate use of antivenom, and patient support have also been controversial. Locating and obtaining appropriate antivenom may be difficult, resulting in critical delays (Seifert, 2006b). Species-specific antivenom should be sought unless there is evidence for cross-species efficacy. Most private collectors do not routinely maintain exotic antivenom (Keyler, 2006). Lack of sufficient appropriate antivenom can be a determining factor in choosing not to accept cases or engage in specific research projects.

Foreign manufactured antivenom can be imported by facilities or individuals under an Investigational New Drug license issued by the Food and Drug Administration, Department of Health and Human Services. These products may be species specific or polyvalent. Some antivenom have shown cross-species neutralization (Minton, 1999; see also AZA website, Antivenom Index), but evidence must be available for cross-species efficacy before relying on this strategy. The appropriate antivenom should be provided by a responsible owner or researcher and travel with the snake to the clinic. If the owner does not have the appropriate antivenom, the nearest source is located prior to arrival. For long-term studies, the acquisition of the appropriate antivenom is recommended.

An online Antivenom Index (AI), a publication of the Association of Zoo and Aquariums (AZA) and the American Association of Poison Control Centers

(AAPCC) lists specific antivenom for treatment of exotic snakebite and their locations across the country. The AI is posted at the AZA website (www.aza.org) in the Members Only section. Regional Poison Control Centers have access to this information and should be consulted when establishing snakebite protocols or locating and seeking access to antivenom. The Miami-Dade Fire Rescue Antivenom Bank (formerly the Florida Antivenom Bank, Inc.) currently stocks a significant inventory of foreign antivenom that are listed on their website (www.miami-dadefirerescue.com).

MANAGEMENT GUIDELINES

Strict protocols for handling, routine husbandry, and staff training promote safety for staff and animals. Written protocols for snakebite response must be in place prior to receiving venomous reptiles. Snakebite protocols and case approach for attending physicians should be established with the local hospital and emergency room physicians to help ensure swift and consistent treatment. A list of consulting physicians who are experts in treating snakebite, should be readily available as a resource for local physicians, as few are familiar with proper clinical treatment of snakebite.

The following venomous reptile handling protocol serves as a baseline for establishing best practices and may be expanded to incorporate unique aspects of facilities or research projects.

- 1. No venomous reptiles should be handled by anyone except designated personnel.
- 2. Staff should be thoroughly trained, knowledgeable, and comfortable with handling procedures.
- 3. Always review techniques and procedures with staff. Set up the work space in advance and clear the area of unnecessary objects or obstacles. Have all appropriate tools readily available.
- 4. Never work with venomous reptiles when in a hurry, mentally distracted, or on medication that may impair alertness.
- 5. Two qualified personnel should always be present. Assistance is often needed and a second person is crucial should snakebite occur.
- 6. Cages should remain locked until they are ready to be opened. Always announce that a cage is to be opened so the attention of support staff is immediately focused on the procedure.
- 7. All cages should be clearly marked "VENOMOUS." An additional label should state the name of the species (common and scientific name), type of antivenom, and number of animals contained.
- 8. Never handle with your hands a reptile that appears dead initially. Always use a tong or snake hook to test for movement. The mouth of a dead specimen should be carefully taped closed to avoid unintentional contact with the fangs.

EQUIPMENT AND METHODS

Venomous reptiles can be managed safely by using the proper tools and techniques. Training and experience play a significant role in developing expertise. A working knowledge of snake behavior and their reaction to stimuli aid in strategizing the best methods to use for a particular procedure. An organized and methodical approach to handling and restraint increases control and is assuring to support staff, who may be unfamiliar with working venomous reptiles. The equipment and methods described here are proven techniques. Innovations can produce further modifications for specific procedures.

Snake Hooks

The manipulation of venomous snakes using snake hooks (Figure 20.2), as opposed to tongs, lowers the potential of injury. Reptiles have a single occipital condyle supporting their skulls upon the cervical spine. Rough handling or improper restraint can cause spinal injury (Frye, 1991) when the snake twists or thrashes. Vertebral morphology and the limitations of movement by vertebrae and axial musculature reviewed are by Gasc (1976). Using tongs for restraint can also induce the snake to bite itself. This can result in self-inflicted fang penetration and envenomation. Although the effects of self-envenomation are usually minimal because of immunity, mechanical damage caused by fang penetration can be serious.

The choice of snake hook is dependent on the size and species. Hooks come in a variety of sizes and configurations and can be home-made or purchased from specialty suppliers (e.g., Midwest Tongs, Greenwood, MO, www. tongs.com; Animal Capture Equipment, Inc., Bacliff, TX, www.ace-cap.com). Two main design aspects need to be considered when choosing the appropriate hook. First, the length of the hook handle must be longer than the striking distance to the hand. In most species this is usually two-thirds the length of the snake or more! The second is that the terminal end of the hook, which supports



Figure 20.2. Snake hooks (top to bottom): Wide blade "python hook," extension hook, double-handled hook, various styles, "L hook" or pinning hook.

the snake, should be of sufficient diameter to comfortably hold the weight of the snake. Large, heavy animals require the wider support surface found on larger diameter hooks. Python hooks have wide flattened surfaces of 3 to 6 cm for added comfort to the snake during lifting. This results especially in a more consistent manipulation of large vipers (genus *Agkistrodon, Bitis, Crotalus, Lachesis,* and *Vipera*). The main disadvantage of python hooks is that they usually lack sufficient shaft length for large specimens. A hook with a terminal L-shaped end is not recommended. The snake will slide down the shaft if it is lifted higher than the handle of the hook. Hooks are relatively simple tools that can be made and tailored to problematic species or individuals.

The following are basic steps when using a hook:

- 1. Always set up all required equipment first (transfer or holding containers, and a clear work area) and review with personnel the procedure steps. It is desirable to have a second potential handler with a hook should assistance be required.
- 2. Always open bags, containers, and cages using proper safety methods.
- 3. The hook tip is initially inserted under the anterior portion of the snake and slid caudally to the midpoint or its approximate center of gravity, on the body side facing the handler.
- 4. Once the hook is at the desired location, lift the snake in one motion, just high enough for the head and tail to clear the surface. This will induce the snake to hold and balance. If it is still moving and not balanced, gently set the animal down and repeat the process.
- 5. Once balanced, lift and move the snake to the desired location. Prevent the head and tail from touching objects during transfer. This will often startle the snake and induce it to come off the hook.
- 6. Gently set the snake down and remove the hook. Be prepared to use the hook to keep the snake under control or to further manipulate it for the intended procedure.

Longer-handled hooks for larger and more agile snakes have a second grip located above the base grip of the hook. Using two hands on the hook, with the second (anterior) grip as a pivot point, aids in lifting heavier specimens while increasing dexterity and control of the specimen. Care must always be taken that the position of the second grip is outside the striking range of the snake.

Some snakes require double-hooking to distribute their weight at two points. This includes very large, massive specimens where support on a single surface will cause discomfort or injury. Snakes with medical problems (e.g., fused vertebrae or a recent surgery) are also supported this way. Active snakes and arboreal prehensile-tailed species are also handled with greater control when double-hooked.

The use of two snake hooks requires more finesse than one.

- 1. Hold a hook in each hand and insert them under the middle portion of the snake, on the same side of the body that faces the handler.
- 2. Move the hooks away from each other to points dividing the snake's length into thirds. While the hooks are being moved to these locations, each hook should be lifted slightly, testing the snake's tendency to balance.
- 3. Once the hooks are appropriate for balance, lift the snake and determine if it is stable. If so, transfer it in a smooth, deliberate movement.
- 4. When lifting, outward pressure (away from the snake's midpoint) of the hooks will help keep tension on the snake and not draw the hooks together if the snake tries to progress forward.

This technique requires practice, but is not difficult. Each snake reacts differently to the double-hooking process. For specimens that benefit from double-hooking, this is an excellent technique and should be used routinely.

Tongs and Forceps

Various styles of snake tongs and forceps (Figure 20.3) are available from reptile equipment dealers (Animal Capture Equipment, Inc. Midwest Tongs). They should not be used as a primary method of restraint owing to their potential to injure. Many snakes thrash or bite the tongs when held tight enough for restraint. Tongs should only be used as a last resort in an emergency. Their use is not an acceptable substitute for lack of training or skill with a snake hook (Altimari, 1998).

Long-handled tongs are ideal when used for feeding, removing cage items, manipulating container lids, holding restraint tubes, and lifting holding bags. Tong

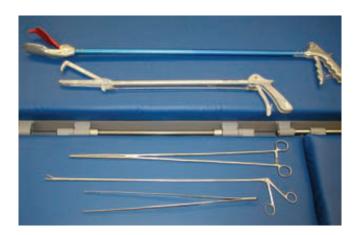


Figure 20.3. Tongs and forceps (top to bottom): Midwest Tong, Pillstrom Tong, hemostatic forceps, endoscopic forceps, and tissue forceps.

length must always be longer than the maximum striking distance of the snake.

Elongated forceps (Figure 20.3) are used for feeding small snakes, removing retained shed or ectoparasites, and assessing depth in anesthetized animals. Forceps length range from 30 to 45 cm. They must be used cautiously when working in close proximity to the head, allowing for potential movement and strike ability.

Shift Boxes

Most snakes enter boxes where they can seek visual and tactile security. Shift boxes are placed either inside the enclosure or attached to the outside. Box size need only be large enough for the snake to lie comfortably in a resting coil. Many prefer to wedge into a tight-fitting space for physical and tactile security. Normally, the snake's head in a shift box is pointed toward the opening, awaiting the passing of potential prey. They commonly strike out at any movement in front of the opening. Training some elapids to enter shift boxes (Kipp, Krebs, and Simmons, 2006) is achieved with classical conditioning techniques. This is a very useful management tool for long-term captive animals requiring routine handling.

Shift boxes are most appropriate for large, swift elapids. They can be designed to attach directly to the cage (Figure 20.4). In snake collections requiring multiple enclosures, the openings in cages, shift boxes, and the points of attachment are standardized so boxes can be interchanged. Cages are also designed with a center divider that allows the handler to shift the snake from one side to the other to facilitate safe servicing. The divider slide space should be sufficiently narrow to prevent escape when the divider is removed.

Shift boxes within a cage (Figure 20.5) should be solid with a bottom and locking door (Rossi, 1995). They are easily fabricated from plywood and sealed with



Figure 20.4. Shift box and interfacing cage for an arboreal snake. Not shown are transparent top and side panels of shift box. (Used for Gold's tree cobra, Pseudohaje goldii, Central Florida Zoological Park.)



Figure 20.5. Shift box in cage. Shift box door can be slid close with a snake hook and locked. Black mamba, Dendroaspis polylepis. (Courtesy of Medtoxin Venom Laboratories.)

polyurethane to facilitate cleaning. A horizontal sliding door is designed to be closed with a hook once the animal is enclosed. A locking pin or mechanism for the shift box door is secured prior to removing from the cage and when transporting the snake.

Many styles and designs for shift boxes that attach to the outside of enclosures have been used to facilitate safe cage servicing or aid in restraint and immobilization for veterinary procedures (Habitat Systems Ltd., www.habitatsystemsltd.com). Historically in zoos and research facilities boxes have been designed and fabricated in-house to fit a specific enclosure for a designated species or individual. Shift boxes have primarily been used for shifting large elapids that are dangerous to work in an open environment using a hook. However, any venomous species is a candidate for shifting to ensure a safe and controlled procedure.

Shift boxes attached to enclosures need to incorporate the following design elements:

- 1. Appropriate comfortable size for the snake
- 2. Sturdy construction, able to endure dropping and long-term use
- 3. Secure method attachment to the enclosure
- 4. Locking slide door that corresponds to the door on the cage
- 5. Large top opening access door (lockable)
- 6. Clear top and/or side section to view the snake
- 7. Adequate ventilation holes
- 8. Sealed surfaces to promote easy cleaning

Variants on the preceding design combine a squeeze for restraint. An interior sliding wall (Figure 20.6) is used to push the snake toward the opening and into the restraint tube. Care is taken to ensure that the restraint tube diameter matches the box opening so no gaps exist. Additionally, the tube and the box must be securely



Figure 20.6. Shift box/squeeze box. Inner panel manually slides toward the entrance hole in the box for tube restraint or against transparent slotted end for injections. (Dallas Zoo, Courtesy of Habitat Systems Ltd.)



Figure 20.7. Shift box/squeeze box. Features include removable squeeze apparatus, slotted end for injections, two capped side ports for tube restraint, and top capped feeding chamber with sliding false floor for protected feeding. Not shown is removable center divider to create "U-maze" to facilitate total entry of long snakes. Jacksonville Zoo and Gardens, black mamba exhibit, Dendroaspis polylepis. (Courtesy of Habitat Systems Ltd.)

attached (usually manually braced) to prevent changes in restraint tube position. Once the snake enters the tube a safe distance, it is grabbed and restrained using a normal tube restraint grasp.

More advanced designs (Figure 20.7) combine features to aid in the husbandry and management of venomous snakes. Optional elements include removable squeeze apparatus with a slotted end panel for injections, capped side ports with interchangeable openings of various diameters for tube restraint, enclosed top feeding chamber with sliding false floor (drops feed rodent into shift box without directly opening the box), and removable center dividers to create a U-maze to



Figure 20.8. Traditional shift box. This simple design enables the snake to shift out of cage eliminating direct contact. Snake can then be transferred for anesthesia or other procedures.

facilitate total entry of long snakes. These features increase control while emphasizing safety.

Some boxes incorporate a built-in restraint shield or framed wire mesh panel that can be pushed down for temporary restraint. A common application of this design using a wire mesh top panel is for king cobras (Ophiophagus hannah) that frequently retain spectacles. This design is also helpful if treatment requires repeated intramuscular injections.

Shift box design is a function of intended use (Figure 20.8). They can be used to accomplish tube restraint and anesthesia using the entrance hole of the box. Variations have been described (Bertram and Larsen, 2004), but the basic design and function remain the same. When using shift boxes the users must know how all doors operate (especially when removing the box and a second snake is in the cage!) along with corresponding locking and safety features. Some boxes are over-designed, increasing the opportunity for an open or unsecured door. Doors and locks are always double-checked visually and for movement prior to assessing that a snake is safely secured.

Unattended boxes that have been removed from the enclosure are placed in larger, secured, and labeled containers to alert staff to the presence of a venomous snake.

Restraint or "Squeeze" Box

These boxes (Quinn and Jones, 1974) are used to restrain movement of a snake for examination, measurement, and radiography. They consist of a box and a clear shield to press the snake against the bottom of the box for temporary restraint (Figure 20.9). Most have been made of wood, but acrylic boxes have the advantage of being able to view the snake from all sides, including the ventrum (Krebs, Curro, and Simmons, 2006).



Figure 20.9. Traditional restraint box for clinical and field applications. Primarily used for injections and measuring. (Western diamondback rattlesnake, Crotalus atrox.)

The size of the box is determined by the snake; it should enable the animal to lay coiled in a normal position. The open top of the box is fitted with an 0.5-cm Plexiglas shield with a center handle that can be lowered to press the snake against a thick foam rubber or other soft material pad.

It is important that the shield closely fits the sides of the box to prevent the snake from wedging its head through a gap. The shield is initially lowered using tongs, then secured by hand once safely in place. Holes are drilled into the shield to facilitate injections. Multiple holes are drilled across the shield since the position of the snake is random. Shields made of diamond mesh expanded sheet metal have also been used (Meredith Whitney, personal communication), but care must be taken to avoid the snake striking and injuring oral areas.

Measurement is accomplished using a dry-erase ink marker to draw a mid-dorsal line equaling the length of the snake. A thin wire is superimposed over the drawn line, then straightened and measured. Map measurers have also been used to trace line lengths.

If a restraint box is to be used for a period of time, holes are drilled through the sides to permit the passage of aluminum rods to hold down the shield (Fowler, 1978). If a restraint box is used for radiology, it must have a locking mechanism for the top acrylic shield. Snakes secured in such a fashion should not be left unattended and placed in a secured, labeled container.

Restraint Tubes

Manual restraint and immobilization of venomous snakes has been described using a wide variety of techniques for a variety of applications. For many procedures, manipulation of venomous snakes without chemical immobilization is desirable for initial examination, medication, and simple procedures including removal of adhered shed, palpation, blood sampling, and sex determination.

Techniques that employ restraint tools as the primary methods of restraint, such as nooses, tongs, strap sticks, bucket restraint (Gillingham, Clark, and Teneyck, 1983), noose tube restraint (King and Duvall, 1984), strap boards (Ward and Harrell, 1978), and manual restraint following pinning with a snake hook are avoided. Although used with some success by professional snake handlers in the venom extraction industry, these methods increase the risk of snakebite for the occasional handler and can injure the snake. Safer methods using clear tubes and shift, restraint, and anesthesia boxes are preferred. These remote handling methods require more time and equipment, but greatly reduce direct contact with the snake. All procedures should optimize protected contact and effective control, thereby insuring handler safety.

The standard for safe handling of venomous snakes is tube restraint (Murphy, 1971). This method minimizes risk to the handler and potential injury to the snake. Clear hollow tubes are available in a variety of acrylic materials. They can be purchased as individual tubes, usually sold in 2-m lengths, of various diameters (McMaster-Carr, Atlanta, GA, www.mcmaster.com). Sets of restraint tubes are also available from some reptile supply companies. Thin-wall, flexible tubes crack easily and, therefore, less safe than thicker-walled tubes. Polycarbonate hollow rods and polyethylene terephthalate (a co-polyester material) with a minimum wall thickness of 0.25 cm are best. These products are more durable and do not break if dropped.

The basic steps for tube restraint are as follows:

- 1. Choose a tube with an inside diameter that will not allow the snake to turn around (inside diameter less than the length of the snake's head or slightly larger than the snake's girth at mid-body).
- 2. Using a hook, place the snake on a smooth surface. Small and medium-sized specimens are worked within a container. This is usually a trash can or other open-top container large enough to facilitate movement by the handler to manipulate the snake into the tube. Large and more sedentary snakes are worked on the floor or ground in field conditions. There must to be ample open space for handlers to maneuver safely around the snake. Containers are preferred because they limit the range of motion and position of the snake.
- 3. Use tongs that are longer than the snake's striking range to hold the tube. Grasp the tube in the middle with the tongs in one hand (usually the left hand for a right-handed person) and slowly lower the open end of the tube toward the snake in a manner that will not induce the snake to strike at the tube. Snakes



Figure 20.10. Tube restraint. Position of primary handler and snake in tube just prior to restraint. (Florida cottonmouth, Agkistrodon piscivorus, Central Florida Zoological Park.)

that strike the open end of the tube may incur oral lesions, primarily associated with the mucous membranes that cover the fangs.

4. Using a hook that is longer than the snake's striking range and held above that point, gently touch or hook the animal to manipulate it into the tube (Figure 20.10). This is a combined maneuver moving the tube and the snake in a fashion that will entice it to enter the tube.

This procedure requires patience! Never hurry and always stay in control of the process.

- 1. The first goal is to get the snake's head inside the opening of the tube. This should be done quickly to reduce the chance of the snake striking.
- 2. Sometimes moving the snake backward with the snake hook will encourage it to move forward, entering the tube.
- 3. Once the snake starts to enter the tube, hold the tube motionless so as not to startle the snake.
- 4. More active snakes require the tube to be "worked down" the body following its undulating movements.
- 5. Once the snake has entered the tube, and is at least halfway in (the tong grasp point on the tube if the tube is grasped in the middle) and still moving forward, lay the hook down (or hand it to an assistant) and with that hand quickly grasp the snake and the end of the tube in which the snake entered (Figure 20.11). This secures the snake in the tube and prevents it from backing out. The other hand is used to grasp and support the animal.

Never overcommit to the grab! If the snake begins to back out of the tube or quickly progresses to the end of the tube, abort the procedure and start over.



Figure 20.11. Tube restraint completed. With large specimens, the primary handler secures the snake and tube while the secondary handler supports and restrains the body. (Florida cottonmouth, Agkistrodon piscivorus conanti, Central Florida Zoological Park.)

- Once restrained, immediately visually check your grasp! Both the tube and the snake should be held firmly to keep the snake from progressing forward or backward.
- 2. Make sure there is not an opening between your fingers and the palm of the hand that could allow the snake to withdraw a body coil and withdraw from the tube.
- 3. With medium to large snakes, the assistant should immediately support and restrain the animal's body once it has been successfully restrained. This permits the primary handler to focus his or her attention on securing the snake while supporting the tube with the other hand.
- 4. If a snake has a large girth at mid-body and a relatively small head, a smaller-diameter tube is inserted down the open end of the tube and over the snake's head to keep it from turning around.

Awake snakes require a controlled release from the restraint tube in the following sequence:

- 1. The primary handler grasps the tube midway with the tongs while maintaining tube restraint with the other hand.
- 2. The snake and tube are placed in a container and angled vertically. The grip on the snake is released and the hand is withdrawn rapidly from the container (and the snake's striking range).
- 3. The primary handler and the assistant pick up hooks for further handling.
- 4. The container is secured and labeled appropriately.

The primary handler and the assistant always review the procedural steps before and during the process



Figure 20.12. Tube restraint directly from a shift box containing a squeeze apparatus. In addition to tube restraint, the body of this 14-ft king cobra (Ophiophagus hannah) is also manually held in the shift box during examination to maintain control of the body. (Central Florida Zoological Park, photo credit Sarah Burke).

to ensure a thorough understanding of roles and expectations.

Many large-bodied pitvipers will attempt to progress up the tube when released. This is avoided to prevent the snake becoming stuck in the tube. While still maintaining manual restraint, these snakes should be pulled down the tube to a safe point near the end prior to release. When released, many snakes quickly withdraw from the tube and immediately strike back at the handler. Alternatively, some species (i.e., elapids) attempt to flee. Handlers need to be prepared to use hooks to keep the snake contained.

Tube restraint can also be accomplished directly from a shift box, facilitated by a squeeze apparatus adapted to the box (Figure 20.12). The diameter of the restraint tube must match the hole in the shift box.

Tube restraint provides the handlers and clinicians a high degree of control during the examination. The snake is advanced to the end of the tube for cranial and oral examination. Various locations along the snake's body can also be examined. Care is taken to keep a significant portion of the anterior body in the tube. Restraint tubes are also used for administering oral medications and force-feeding (Radcliffe, 1975). The major advantage of this technique is that the snake is restrained without grasping the head, and the animal is positioned in a relative straight line to facilitate examination, medication, tube-feeding, and anesthesia.

A variation of acrylic tube restraint (Mauldin and Engeman, 1999) employs wire mesh cable holders as the restraint "tube". Although this method can be used with some snakes, it is not recommended for venomous species because they will bite through openings in the mesh, resulting in either envenomation of the handler or oral trauma to the snake.

Restraint Tube Modifications

Clear acrylic restraint tubes can be modified for the needs of the clinician. Tubes are cut to various lengths to facilitate safe handling (i.e., longer tubes for longer snakes). Tubes are drilled to create access holes and elongate cutouts are made for increased access for minor procedures. Appropriately sized PVC caps, rubber stoppers or wooden corks are temporarily or permanently secured at one end to prevent the snake from progressing through the tube.

Care is taken when any opening is made along the length of the tube to prevent hands and fingers from crossing these openings. Many species are capable of biting and protruding a fang through these openings. Bite attempts on the inside of the tube will release venom that will run down the inside of the tube to the hand. Handlers should wear latex gloves to prevent venom contact with the skin that may lead to envenomation through microcuts. All tubes must be thoroughly washed and disinfected immediately after use.

Anesthesia Boxes

Full clinical examination and surgical procedures require chemical immobilization and anesthesia. This is essential when evaluating cranial features such as the nostrils, infraorbital pits, spectacle and eyes, oral cavity, glottis, and tongue. More general procedures such as blood sampling, examination of the integument, removing adhered shed skin, removal of ectoparasites, cloacal examination and sampling, and palpation may be performed employing tube restraint. Radiology may be performed on snakes in shift boxes, squeeze boxes (through a fixed acrylic shield) or through bags if the specimen is inactive. If an intended procedure presents a safety concern for personnel, full chemical immobilization is strongly recommended. Some snakes can be induced in restraint tubes with propofol administered into the ventral coccygeal vessels.

A variety of containers for venomous snakes can be used as inhalant anesthesia boxes. Large clear plastic Rubbermaid® or SteriLyte® storage boxes (Figure 20.13) are available from retail stores. Snakes are placed directly into these boxes only if the lids can be secured to prevent escape. Transparent containers allow observation of the snake during anesthetic induction. A snake contained in a cloth snake bag may be placed inside an anesthesia box. However, judging anesthetic level will depend on evaluating declining bag movement. When testing the movement of a snake inside a bag, always use instruments (forceps, tongs) and never manually palpate the bag.

A snake contained in a shift box or ventilated restraint box can also be placed in an anesthesia box. The anesthesia box, fitted with an adaptor for the breathing system, allows for infusion of the inhalant anesthetic in oxygen from the machine. A shift box may also be enclosed in a plastic bag for administration of inhalation anesthetic through the opening. However,



Figure 20.13. Anesthesia box. A clear plastic storage box fitted with an adaptor to receive the corrugated breathing tube from the anesthesia machine. The transparent container facilitates viewing to judge level of induction. (Rhinoceros viper, Bitis nasicornis, Central Florida Zoological Park.)

induction is very difficult to evaluate when the snake is enclosed in two containers.

Guidelines to assess whether a snake is safely anesthetized include lack of response to tactile stimulation, inhibition of tongue flicking, and lack of ability to right itself when turned over on its dorsum. Snakes can hold their breath for 15 to 20 minutes and anesthetic induction can be prolonged. Once anesthetized, a restraint tube is placed over the head and anterior portion of the body as a secondary safety precaution and the snake is then carefully removed from the box. For continued delivery of inhalant anesthetic either a cover can be fitted over the open end of the restraint tube, a mask placed directly over the head if removed from a restraint tube, or an endotracheal tube is inserted through the snake's glottis and into the trachea.

Transport

Safe transport and receiving of venomous reptiles requires planning and setting up the appropriate equipment in advance. Securing the snake in a cloth bag and placing it in a ventilated locked box is recommended. The cloth bag should be of tight-woven, strong material that allows for good ventilation. Bags are examined for small holes that may be tested by the snake and enlarged, leading to escape. Bags are turned inside out so the seam is on the outside to avoid entanglement in loose threads. Only one animal should be contained in each bag to eliminate defensive striking and facilitate removal. Bags should be long (deep) enough to be easily knotted at the open end and additionally secured with strong tape or plastic cable ties.

To place a snake in a bag, it is hung inside an empty container and secured in an open position using clips (clothes pins work well). Tongs are used by an assistant to hold the sides of the bag open. They are then used to close after the snake is guided in by a hook. Commercially available "snake baggers," long-handled rods with an attached and removable bag, increase safety in the bagging process (Bag-Em™, Animal Capture Equipment, Inc.; Snake Bagger®, Midwest Tongs). Never be too anxious to manually close the top of the bag. Most snakes tend to climb upward after being dropped into the bag. Always visually know where the snake is. Use tongs to close and secure the bag prior to twisting the top down for knotting.

When knotting, first transfer the bagged snake to a flat surface. Place the hook shank across the twisted neck of the bag and pull to secure the snake in the far end of the bag. The bag is secured with strong tape or cable ties either side of the knot. This must be done away from the portion holding the snake. Bags are labeled to identify the snake species with a noticeable VEN-OMOUS notation made on the label. Red labels with the skull and crossbones symbol for poison are most effective. Tongs are used to clamp the bag just under the knot for lifting. Bags should always be carried above the knot and away from the handler's body. Bagged snakes are placed in a suitable container or box while waiting for procedures or transport. Transport boxes containing more than one bagged snake have solid dividers to eliminate the potential for snakes biting each other.

Transport boxes are locked, well ventilated, and kept away from temperature extremes. Boxes are kept out of the sun and transported in air conditioned vehicles to avoid hyperthermia. Boxes are clearly labeled CAUTION: VENOMOUS SNAKES and stored in locked rooms while awaiting transport.

The same level of caution used in bagging the snake must be used during removal from transport containers. Open the transport box as if the snake inside has escaped the containment bag. Keep fingers and hands away from openings (use tongs) and be prepared to hook a snake into a holding container. The bag is removed from the container using tongs. Snakes will bite through cloth bags induced by limited visual capability or when the bag is touched. Bites through either bags or screened surfaces can result in envenomation. A snake's fangs can become hung up in the bag material and may expel larger quantities of venom while freeing itself then present in a defensive bite.

Prior to opening the bag is placed on a flat surface and the hook shank is positioned to secure the snake in the end. All extremities are held safely away from this portion of the bag. Once untied, tongs are used to secure the open bag end. It is then picked up and lowered into a container. The snake is released by picking up the bottom end of the bag with the tongs. Bags with a hem line sewn across the corners provide an area of material to grab without pinching the snake.

A field transport box (Birkhead et al., 2004) for carrying large numbers of venomous snakes combines both

tube restraint and a modified transport container. In this design, 10 polyethylene restraint tubes, capped at both ends, are secured by spacers in a transport container. The advantage of this design is individual containment of each snake that is positioned for immediate manipulation or restraint.

The International Air Transport Association (IATA) publishes Live Animal Regulations that are adopted by most airline carriers. When shipping air freight, it is prudent to review these regulations in case airline employees question the design and features of the shipping crate and the methods by which the snakes are contained. IATA requirements (for snakes see Part 8, Container Requirement #44) are presented as examples to be adopted depending on the species and size of the snake. Specific suggestions in the IATA regulations include container rigidity, packing material, size and type of container, specification for snake bags, doublebagging snakes with a transparent mesh inner bag for inspection, wire-covered containers, and an abbreviated listing of venomous snakes and some colubrids that are considered venomous. It is the responsibility of the shipper to ensure that materials and methods are appropriate for safe transport. It is rare that an airline employee will ask the shipper to open a container of venomous snakes for inspection. This is not the case for international shipments that are routinely inspected by wildlife customs agents monitoring CITES regulations for international trade of listed species.

VENOMOUS LIZARD MANAGEMENT

Gila Monsters and Beaded Lizards (Helodermatidae)

Venomous lizards known to produce significant envenomation in humans are restricted to two species, the Gila monster (*Helododerma suspectum*) and the Mexican beaded lizard (*Heloderma horridum*). As studies continue on the evolution of reptilian venom systems (Fry et al., 2006) additional "non-venomous" lizard taxa will be recognized as having toxin-secreting oral glands. Currently this is restricted to some species of monitor lizards (e.g., the desert monitor) (Ballard and Antonio, 2001).

Helodermatids are large, stout-bodied lizards with large heads, powerful jaws, and short legs adapted to digging. They are easily recognized by their colorful, intricate skin patterns, and rounded tuberculate scales that give them a beaded appearance. Adult Gila monsters average 36 cm, whereas beaded lizards can reach 1 m in total length.

Helodermatids have evolved "defensive venom" tailored to create significant pain to ward off predators. Bites are extremely painful and can have systemic effects, including a rapid drop in blood pressure that may result in hypotensive shock (Preston, 1988). Unlike snakes, the venom glands of helodermids are mandibular and



Figure 20.14. Pre-restraint position for helodermatids. Head should be immobilized prior to manual restraint. (Gila monster, Heloderma suspectum, Central Florida Zoological Park.)

appear as a rounded swelling located midway on the lower jaw. The large triangular-shaped head is the result of well-developed musculature associated with biting and maintaining a vice-like grip. When biting, helodermatids exhibit a pumping action of the jaw musculature while embedding the enlarged, grooved, venom conducting teeth, located above the venom glands. Many accounts of severe gripping bites result in the use of pliers, crow bars, and decapitation to disengage the lizard from the bitten extremity. Severity of envenomation is a function of the amount of time the lizard is allowed to bite. Envenomation is treated symptomatically as there is no antivenom for helodermatids.

Helodermatids are deceptive, normally exhibiting slow movements and a sluggish behavior, but are capable of swift lateral and upward movements of the head and upper body when attempting to bite. Of 21 venomous bites received by zoo workers over a 25-year period (Card and Roberts, 1996), four were inflicted by helodermatids. They concluded that because they are generally considered relatively benign captives, this assumption misleads individuals to handle them carelessly. No matter how much their owner professes its tameness, all helodermatids should be handled with the same care as for venomous snakes.

Manual restraint requires first pinning the head down on a flat surface with a snake hook or pinning bar prior to restraint (Figure 20.14). Once secured, they are picked up with a firm grip at the base of the head and a forelimb held between the fingers to maintain control of the upper body. Once elevated, the second hand is used to support and hold the body (Figure 20.15).



Figure 20.15. Helodermatids can be manually restrained by securing a firm grip at the base of the head with a forelimb held between the fingers to maintain control of the upper body. Once elevated, the second hand is used to support and hold the body. (Gila monster, Heloderma suspectum, Central Florida Zoological Park.)

Locking hemostats (40–60 cm) have also been used to successfully pin helodermatids (Poulin and Ivanyi, 2003) by using the interlocking base portion (area between the finger eyelets) as the pinning bar.

Helodermatids can be closely examined using manual restraint. Examination of the oral cavity using a hard rubber speculum has limited use because they will vigorously bite down on any object placed in its mouth.

Helodermatids can be anesthetized by administering an inhalant anesthetic into an induction chamber. Anesthetized helodermatids should again be pinned as described before removal from the anesthetic chamber. One of the last reflexes to be lost is the defensive bite.

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21

Chelonians (Turtles, Tortoises, and Terrapins)

Juergen Schumacher

INTRODUCTION

Worldwide, chelonians are threatened by loss of habitat, human consumption for food, and collection from the wild for the international pet trade. Although a variety of tortoise and turtle species are successfully exhibited and bred in zoological collections, many are listed as endangered or threatened in the wild (Boyer and Boyer, 2006). Both infectious and non-infectious diseases affect free-living and captive chelonian populations. Studies assessing health and disease, especially in wild populations, and medical and surgical treatment of captive chelonians have made considerable advances over recent years. A safe and effective anesthetic protocol is essential for a variety of procedures in both field and hospital conditions. Invasive surgical procedures should be performed in a veterinary hospital equipped with sterile surgical facilities, inhalational anesthesia machines, and monitoring equipment. However, under field conditions the need for short-term anesthesia, often with injectable anesthetic agents, arises for collection of diagnostic samples such as biopsy specimens.

Design of a safe and effective anesthetic regimen, including selection of effective drugs and dosages, is often challenging in chelonians (tortoises, turtles, and terrapins) because of their unique anatomy and physiology. Chelonians, especially aquatic animals, commonly exhibit species and individual differences in response to anesthetic drugs, dosages, and protocols. It is a prerequisite to have a good knowledge of normal anatomy, physiology, and the pathophysiology of their diseases to select a safe and effective protocol. Tortoises, turtles, and terrapins, with the exception of leatherback sea turtles (family Dermochelyidae), are poikilothermic, indicating that all body functions are dependent on environmental temperature. Thermoregulation in a healthy animal is accomplished by behavioral adaptations; however, sick turtles and tortoises often fail to effectively regulate their body temperature. The response to anesthetic drugs, as well as cardiopulmonary performance during anesthesia, is optimal if the patient is maintained within the species-specific preferred optimal temperature range.

Studies have investigated the effects of a variety of anesthetic and analgesic agents. However, little information has been published on the effects of these drugs on cardiopulmonary performance. Information on the pharmacokinetics and effectiveness of analgesic agents in commonly exhibited chelonian species is scant. This chapter emphasizes anesthetic and analgesic techniques in turtles, tortoises, and terrapins, other reptiles are covered in Chapters 19 and 20 or in reviews published elsewhere (Bennett, 1991, 1996; Heard, 1993, 2001; Page, 1993; Schumacher, 1996; Schumacher and Yelen, 2006).

BIOLOGY, ANATOMY, AND PHYSIOLOGY

The order Chelonia is one of four in the class Reptilia and includes over 270 species of turtles, tortoises, and terrapins. Most are aquatic or semi-aquatic with the highest number of species found on the North American continent. Worldwide, chelonians are found in tropical as well as temperate regions and inhabit diverse habitats ranging from deserts to tropical rainforests. They differ considerably in size, ranging from the 0.1 kg Cape tortoise (*Homopus* spp.) to the approximately 1,000 kg leatherback sea turtle (*Dermochelys coriacea*) (Raphael, 2003).

Anatomy and physiology differ from mammalian and avian, as well as other reptiles. Chelonians have a bony shell, divided into the carapace and plastron, and covered by keratin scutes. Some species have hinged plastrons (e.g., box, *Terrapene* spp., and mud, *Kinosternon* spp., turtles) or carapaces (e.g., hinged-back tortoises, *Kinixys* spp.). In general, aquatic species have smaller plastrons compared with terrestrial species and are often unable to completely withdraw their head, neck, and limbs into the shell.

The structure and function of the respiratory system differs considerably from other reptiles, and between

terrestrial and aquatic species (Perry, 1998; Wang, Smits, and Burggren, 1998; Murray, 2006a). Chelonians lack a functional diaphragm and the force to move air during inspiration and expiration comes from movement of the abdominal as well as pectoral and pelvic musculature, resulting in intrapulmonary pressure changes. A septum horizontale, dividing the thoracic from the abdominal cavity, is found in most, with the exception of marine turtles. Inspiration is passive, whereas expiration is actively achieved by increasing intrapulmonary pressure (Boyer and Boyer, 2006). All chelonians move air through the nares during inspiration and expiration. Open-mouth breathing is always a sign of respiratory tract disease, usually obstruction of the upper airway. The glottis is located at the base of the tongue and good jaw relaxation is essential for visualization. Chelonians have a short trachea with complete tracheal rings. The bifurcation into the left and right intrapulmonary bronchus is located at the level of the thoracic inlet. The relatively rigid, paired, multi-chambered lungs are located directly underneath the carapace. They have high compliance values and although the volume is larger than in a mammal of comparable body size, the surface area for gas exchange is smaller (Perry, 1998).

Respiratory physiology differs considerably between terrestrial and aquatic species. In all, the lungs are the major organs for gas exchange. However, some aquatic species are capable of cutaneous and cloacal gas exchange, primarily for the elimination of CO₂. During long periods of apnea, aquatic species convert to anaerobic metabolism. Chelonians increase the minute volume by increasing the respiratory rate. Respiration is controlled by environmental temperature as well as hypoxic and hypercapnic events. They increase ventilation through specific receptors sensitive to low O₂ and high CO₂ concentrations. Hypercapnia increases tidal volume, whereas hypoxemia increases respiratory rate. Respiratory rate also increases during hypercapnia, but decreases during hyperoxemia (Wang, Smits, and Burggren, 1998). An increased oxygen demand during high temperatures, or following prolonged dives in aquatic species, is met by increasing tidal volume and not respiratory rate. In an oxygen-enriched environment (e.g., 100% oxygen delivered via endotracheal tube during recovery from anesthesia), chelonians decrease respiratory rate and tidal volume. Therefore, it is indicated to assist ventilation in the recovery period with room air. Intrapulmonary shunts occur in most species, and represent a portion of pulmonary blood bypassing gas exchange, thus reducing the efficiency of pulmonary gas exchange. This results in reduced arterial PO₂ concentrations (Wang, Smits, and Burggren, 1998). In red-eared sliders (Trachemys scripta) progressive hypoxemia resulted in increased ventilation and tachycardia. Hypercapnia increased ventilation, but did not alter heart rate. It was concluded these turtles alter

intracardiac shunting to increase pulmonary perfusion in response to hypoxia (Herman and Smatresk, 1999).

Chelonians have a three-chambered heart; two atria and a single ventricle (Murray, 2006b). Muscular ridges within the ventricle, as well as the timing of contractions, result in a functional separation of the ventricle. This prevents mixture of well-oxygenated blood from the lungs and poorly oxygenated blood from the systemic circulation. Atrioventricular valves prevent regurgitation during ventricular systole and muscular ridges form a functional ventricular septum by approaching the ventricular wall (White, 1968). Heart rate depends on body size, metabolic status, and environmental temperature. Most anesthetic drugs have cardiovascular depressant effects.

PRE-ANESTHETIC CONSIDERATIONS AND MANAGEMENT

A complete history, visual and physical examination is essential to formulate a safe and effective anesthetic protocol. Patient history is reviewed, including husbandry and environment, and onset of clinical signs of disease. A visual examination includes body condition and shell, hydration and nutritional status, presence of trauma, and clinical signs of infectious disease (e.g., viral, bacterial, and/or fungal). Physical examination includes a systematic evaluation of all body organs, and includes recording the body weight to ensure accurate drug dosage calculations. The patient is stabilized prior to induction and if indicated, fluid therapy, nutritional support, and treatment of underlying diseases are initiated. Chronic respiratory disease is common and may affect response to anesthetic drugs. Respiratory tract disease is evaluated based on respiratory rate and depth, nasal discharge, culture, and sensitivity testing and radiography (Schumacher, 2003). Baseline respiratory and heart rates are measured and recorded before induction.

A venous blood sample is collected prior to anesthesia for determination of hematological and plasma biochemical values. Blood reference ranges have been described, but they vary with species, age, season, and metabolic status. In small species, minimally the packed cell volume, total protein, and blood glucose levels are determined. Additional diagnostic tests may include fecal screens for enteric parasites, collection of biopsy specimens, and aspirates for cytological and microbiological evaluation. In most chelonians, radiography and ultrasonography do not require general anesthesia.

Prior to anesthesia, the patient is ideally acclimated to temperature and humidity levels appropriate for the species; for most a temperature range of 22°C to 28°C. Fluid therapy to restore homeostasis is initiated if there is indication of volume depletion based on physical and laboratory findings. Fluid requirements and selection, as well as treatment of disturbances of hydration status,

have been described by the author (Schumacher, 2000). Constant rate infusion of a balanced electrolyte solution is preferable over intermittent boluses. Venous access is attained with either an intravenous (IV) or intraosseous (IO) catheter. If venous access is not possible, fluids can also be administered intracoelomically or subcutaneously. In patients with identified electrolyte imbalances, the underlying problem is identified and treated. Blood electrolyte levels are similar across species, but can vary depending on species and environment (aquatic vs. terrestrial). Although regurgitation is seldom encountered, the author recommends pre-anesthetic fasting because many anesthetic drugs are associated with pronounced temporary gastrointestinal stasis (ileus).

Appropriate and effective analgesic therapy is initiated in animals diagnosed with pain and discomfort upon presentation. Administration of effective analgesic agents is part of a pre-emptive analgesic regimen.

The IV route of administration of anesthetic drugs is most effective. However, if there is no IV access, intramuscular (IM) administration of sedative and anesthetic agents may be necessary. In chelonians oral and subcutaneous (SC) administration of anesthetic drugs is unreliable and results in prolonged and unpredictable induction and recovery times. A renal portal system is present, but it appears to minimally affect the pharmacokinetics of drugs injected into the caudal half of the body (Holz et al., 1997; Benson and Forrest, 1999).

In most chelonians, IM injections are administered into the forelimbs, if a limb can be extracted from the shell. However, irritant drugs (e.g., ketamine) injected distal to the carpus will cause necrosis and potential loss of a limb. Therefore, injections are administered into the deep pectoral muscles on the inside surface of the plastron.

Depending on patient size, the jugular vein can be catheterized for intravenous access or the coccygeal vein can be used for collection of a venous blood sample. The subcarapacial vein can also be used for collection of venous blood samples and administration of IV drugs. In small chelonians, the ventral or dorsal coccygeal vein is unsuitable for IV drug administration.

PHYSICAL RESTRAINT AND PREMEDICATION

Chelonians are often more difficult to handle than other reptiles because of their ability to withdraw their limbs, head, and neck into a shell. Although aquatic turtles, especially marine, are unable to withdraw completely into the shell, they are capable of inflicting a serious bite to the inexperienced handler if the head is not secured. Large chelonians and small species that have retracted into the shell require IM sedatives to facilitate handling, collection of diagnostic samples, and to gain access to a peripheral vein for IV drug administration. The type and amount of preanesthetic drugs

required to facilitate handling and administration of inhalational or injectable agents for induction and maintenance of anesthesia, depends on the health status of the animal as well as the procedure to be performed. Perioperatively, chelonians scheduled to undergo a surgical or potential painful procedure are administered an analgesic agent (e.g., butorphanol or buprenorphine) as part of a balanced anesthetic regimen. Administration of an analgesic will provide intraoperative and post-operative analgesia and may reduce inhalant anesthetic requirement. However, in green iguanas (Iguana iguana) butorphanol does not have significant isoflurane-sparing effects (Mosley, Dyson, and Smith, 2003a). The cardiac anesthetic index of isoflurane in green iguanas is greater than 4.32 and not affected by the administration of butorphanol (Mosley, Dyson, and Smith, 2003a). In most chelonians, butorphanol and buprenorphine alone have minimal to moderate sedative effects even when used at high doses (greater than 1 mg/kg). Similarly, benzodiazepines alone (i.e., midazolam, diazepam) have minimal sedative effects. If venous access has been established, midazolam IV will reduce the amount of the induction drug (e.g., propofol) necessary to induce anesthesia. Midazolam (1.5 mg/kg IM) was effective in immobilizing red-eared sliders for minor manipulations (Oppenheim and Moon, 1995). However, benzodiazepines are rarely used alone and are most commonly combined with dissociative agents (i.e., ketamine) and opioids (i.e., butorphanol, buprenorphine). The author does not routinely use anticholinergic agents (i.e., atropine, glycopyrrolate) to reduce respiratory secretions.

Effective pain management in common reptile species, particularly chelonians has not been well described and analgesia for the chelonian patient is often not provided (Read, 2004). Reptiles and mammals may have different pathways of pain and receptors, although an endogenous opioid system and nociceptive neurons have been described in reptiles (Machin, 2001). The pathophysiology of pain has been described previously (Robertson, 2001; Muir, 2002a). Acute and particularly chronic pain has detrimental effects on the patient's metabolism, and may result in compromised immune function as well as hematological and biochemical imbalances (Muir, 2002b). Signs of pain and discomfort in a chelonian include restlessness, increased respiratory rate, anorexia, lethargy, and abnormal body position. However, recognition of normal and abnormal behavior is often challenging in chelonians (Bradley, 2001).

Prevention of pain is most effective and pre-emptive analgesia is recommended in all chelonians scheduled for surgical procedures. Balanced analgesic techniques, including administration of systemic (opioid agents) and long-acting local anesthetic agents (e.g., bupivacaine) are most effective. Local anesthetic agents (e.g., lidocaine

up to 10 mg/kg, bupivacaine up to 4 mg/kg), for the provision of topical and regional anesthesia may be administered directly into surgical sites (e.g., abscess debridement) or plastronotomy fields (Mader, 1998). In chelonians, management of acute pain (e.g., shell repair, plastronotomy) is best achieved by administration of opioid agents such as butorphanol and buprenorphine. Treatment of chronic pain (e.g., neoplasia, renal disease) in chelonians is challenging owing to little knowledge of the effects and side effects of drugs commonly used in domestic animals. Non-steroidal anti-inflammatory agents (e.g., ketoprofen, carprofen, meloxicam) may be useful for the treatment of chronic pain in chelonians; however, they should not be used in animals with gastrointestinal disease and impaired renal function.

INJECTABLE ANESTHETIC DRUGS

Injectable anesthetic drugs have been used and investigated for induction and maintenance of anesthesia in chelonians (Table 21.1). Most agents, especially when used alone at high dosages, cause pronounced cardiopulmonary depression, prolonged induction and recovery times, and poor muscle relaxation during maintenance of anesthesia. In chelonians, species and individual differences are commonly seen in response to parenteral anesthetic agents.

Ketamine

Ketamine HCl is used in chelonians for both immobilization and induction of anesthesia. It has a wide

margin of safety and can be administered IM for immobilization and IV for induction of anesthesia. Ketamine alone provides poor muscle relaxation, minimal analgesia and, if used at high dosages, prolonged recovery times. Although not reported in chelonians, studies in snakes have shown that ketamine alone produces respiratory depression, hypertension, and tachycardia (Schumacher et al., 1997). Ketamine is rarely used alone because high dosages are required in most species to produce immobilization. Most commonly, ketamine is combined with benzodiazepines (i.e., diazepam, midazolam), opioids (i.e., butorphanol, buprenorphine) or the α_2 -adrenergic agonist medetomidine. A combination will reduce the ketamine dose; this results in more rapid and smoother induction and recoveries, improves muscle relaxation, and provides analgesia. However, in red-eared sliders high-dose ketamine (60 mg/kg IM) alone or in combination with xylazine (2 mg/kg IM) or midazolam (2 mg/kg IM) produces variable sedation (Holz and Holz, 1994).

Tiletamine/Zolazepam (Telazol)

Tiletamine/zolazepam (Telazol) can be used for immobilization and induction of anesthesia. At high dosages (greater than or equal to 6 mg/kg IM) it is associated with prolonged recovery (greater than or equal to 48–72 hrs), especially in African spurr-thighed tortoises (*Geochelone sulcata*), and is not recommended by the author. To facilitate handling of large chelonians (i.e., to gain access to a peripheral vein) a low dose of tiletamine/zolazepam (2–4 mg/kg IM can be used. However, induction with propofol is then recommended.

Table 21.1. Anesthetic, local anesthetic, and analgesic drugs used in chelonians (tortoises, turtles, and terrapins).

Drug	Dosage(mg/kg)	Route	Frequency	Comments
Bupivacaine	1-2	Local infiltration	4–12 hr	Long-acting, maximum dose: 4 mg/kg
Buprenorphine	0.02 - 0.2	SC, IM	12-24 hr	All species
Butorphanol	0.4-2	IM, IV	12-24 hr	All species
Carprofen	1-4	PO, SC, IM, IV	24 hr	All species
Diazepam	0.2-1	IM, IV	_	All species
Flunixin meglumine	0.5-2	IM	12-24 hr	All species
Isoflurane	Induction: 4%–5%	Endotracheal tube	_	Inhalational agent of choice, all species
	Maintenance: 2%–3%			
Ketamine	2-30	IM, IV	_	All species, low dose for IV
Ketoprofen	2.0	SC, IM	24 hr	All species
Lidocaine	2-5	Topical and local infiltration	_	Maximum dose: 10 mg/kg
Medetomidine	0.03-0.15	IM	_	Species variability
Meloxicam	0.1-0.2	PO	24 hr	All species
Midazolam	0.5-2	IM, IV	_	All species
Morphine	0.4-2	SC, IM	12 hr	Species variability
Oxymorphone	0.1 - 0.2	SC, IM	12-24 hr	Species variability
Propofol	2-5	IV, IO	_	Injectable induction agent of choice
Sevoflurane	Induction: 7%–8% Maintenance:	Endotracheal tube	_	Species variability, rapid induction and recovery
mu	2.5%-4.5%			
Tiletamine/zolazepam	2–4	IM, IV	_	Species variability, prolonged recoveries

Medetomidine

Medetomidine facilitates handling and concurrent administration of synergistic agents results in a plane of sedation effective for short procedures such as abscess debridement, shell repair procedures, and collection of diagnostic samples. It is most commonly combined with ketamine and an opioid (e.g., butorphanol). For reversal, atipamezole is administered IM at 5 times the medetomidine dose. In desert tortoises (Gopherus agassizii) medetomidine (150 µg/kg IM) has produced sedation. However, it produced pronounced cardiopulmonary depression, including bradycardia, bradypnea, and hypotension (Sleeman and Gaynor, 2000). In gopher tortoises (Gopherus polyphemus) a combination of ketamine 5 mg/kg/medetomidine (0.1 mg/kg, IV) also produced short-term immobilization adequate for minor procedures (Dennis and Heard, 2002). This combination was also associated with moderate hypoxemia and hypercapnia, as well as hypertension. Therefore, it is recommended to provide supplemental oxygen and assist ventilation when using this combination. Administration of atipamezole IV to antagonize the effects of medetomidine induced severe hypotension (Dennis and Heard, 2002).

Propofol

Propofol has been used in a variety of reptile species for both induction and maintenance of anesthesia (Bennett et al., 1998; Anderson, 1999; Nevarez, Mitchell, and Wilkelski, 2003). It must be administered IV and the induction dosage depends on the health status of the chelonian and the type and amount of premedication. Propofol causes systemic hypotension, decreased myocardial contractility, and respiratory depression. Propofol (2 to 5 mg/kg IV) induces general anesthesia, especially following premedication with midazolam (0.5 to 1 mg/kg IV). A rapid bolus injection is commonly accompanied by apnea (Bennett et al., 1998). Therefore, it is slowly titrated to effect in chelonians. An IV catheter is placed for anesthetic maintenance with either constant rate infusion (0.3–0.5 mg/kg per minute) or intermittent boluses (0.5-1 mg/kg).

Local Anesthesia

Although not routinely used in chelonians, local anesthetic administration follows the same indications as in domestic animals (Mader, 1998; Schumacher and Yelen, 2006). Agents such as lidocaine or the longer-acting bupivacaine can also be administered concurrently with systemic analgesic agents (Table 21.1). Techniques for local and regional anesthetic techniques, including epidural anesthesia have not been described in chelonians. Interpleural administration of local anesthetic agents is indicated for plastronotomies in chelonians. The most effective long-acting local anesthetic agent is bupivacaine (1 to 2 mg/kg). Administration of bupivacaine is repeated every 4 to 12 hours if the patient will tolerate it. Additional indications for the application of

local anesthetic agents in chelonians include orthopedic and shell repair procedures in combination with systemic analgesic agents.

INHALATION ANESTHETICS

Most anesthetic regimens are based around inhalation anesthetics (Table 21.1). In most chelonians, isoflurane or sevoflurane is administered either alone for induction and maintenance or following a combination of parenteral agents such as dissociative agents, benzodiazepines, opioid agents, and/or α_2 -agonists. Isoflurane or sevoflurane should be administered with a precision vaporizer and a non-rebreathing system is indicated for most chelonians (less than 10 kg body weight). Induction and maintenance requirements of isoflurane or sevoflurane depend on the health status of the chelonian and the degree of sedation following administration of preanesthetic agent(s). Pronounced species differences in response to sevoflurane are apparent in chelonians.

Isoflurane results in short recovery times and minimal cardiopulmonary depressant effects, and has limited effects on renal and hepatic function. For anesthetic induction, most require isoflurane concentrations of 5% and maintenance requirements range between 2% and 3%. The minimum alveolar concentration (MAC) of isoflurane has not been determined in chelonians; in green iguanas the MAC is 2.1% (Mosley, Dyson, and Smith, 2003b). Lower concentrations are indicated in severely debilitated chelonians. Sevoflurane has been investigated as an inhalational agent for induction and maintenance of anesthesia in several reptile species, including chelonians (Rooney et al., 1999; Hernandez-Divers et al., 2003, 2005). In the species investigated, sevoflurane resulted in short induction and recovery times and good muscle relaxation, and facilitated rapid changes in the depth of anesthesia because of its low solubility in blood. In chelonians induction times with sevoflurane vary among species and some species may fail to reach a surgical plane of anesthesia, even at high concentrations. Administration of sevoflurane to desert tortoises (Gopherus agassizii) resulted in minimal cardiopulmonary depressant effects (Rooney et al., 1999). If used alone, most chelonians require sevoflurane concentrations of 7% to 8% for induction and 2.5% to 4.5% for maintenance of a surgical plane of anesthesia.

Nitrous oxide can be administered at a ratio of 2:1 with oxygen and reduces the amount of isoflurane or sevoflurane necessary to induce and maintain a surgical plane of anesthesia. In addition, muscle relaxation is improved and recovery time is shortened with nitrous oxide.

ANESTHETIC INDUCTION AND MAINTENANCE

Induction of anesthesia is challenging in large chelonians and even small species if the limbs and neck are

withdrawn into the shell. Large aquatic species, such as snapping turtles and marine turtles, are capable of delivering a painful bite and may cause serious injury. Most chelonians, except severely debilitated animals, require administration of a sedative agent(s) (e.g., midazolam, 1 to 2 mg/kg IM, and butorphanol, 1 to 2 mg/kg IM) to facilitate handling and gain venous access. Ketamine given alone IM requires high dosages, resulting in prolonged induction and recovery times, poor analgesia, and inadequate muscle relaxation. A combination of ketamine (4-10 mg/kg), butorphanol (0.5-1 mg/kg), and medetomidine (30–150 µg/kg) can be administered IM to facilitate handling. In most this combination facilitates endotracheal intubation and maintenance of anesthesia with isoflurane or sevoflurane (Lock, Heard, and Dennis, 1998). If venous access (jugular vein or coccygeal vein) has been established the author prefers administration of propofol following midazolam (0.5-1 mg/kg IV) for induction of anesthesia. Propofol should be titrated to effect and should not exceed a total dose of 2 to 5 mg/kg IV. Anesthetic induction with inhalational agents alone often results in prolonged induction times, especially in aquatic chelonians capable of prolonged breathholding, and in chelonians without prior administration of sedative agents (Moon and Hernandez Foerster, 2001).

Loggerhead sea turtles were safely induced with an IV combination of ketamine (5 mg/kg) and medetomidine (0.05 mg/kg), and maintained with sevoflurane (0.5%–2.5%) (Chittick et al., 2002). In snapping turtles (*Chelydra serpentina*) a combination of ketamine (20–40 mg/kg IM) and midazolam (2 mg/kg IM) resulted in sufficient sedation to facilitate safe handling (Bienzle and Boyd, 1992). In red-eared sliders alphaxalon/alphadolon (24 mg/kg intracoelomically) resulted in surgical anesthesia in all turtles (Hackenbroich, 1999).

In gulf coast box turtles the reversible neuromuscular blocking agent rocuronium (0.25–0.5 mg/kg IM) induced short-term immobilization sufficient for endotracheal intubation. At the end of anesthesia, the effects of rocuronium were reversed with neostigmine and glycopyrrolate (Kaufman et al., 2003). A chelonian immobilized with a neuromuscular blocking agent is not anesthetized; no analgesia is provided and handling should be kept to a minimum to avoid undue stress on the animal.

Following induction the animal is intubated to facilitate control of the airways and allow for positive pressure ventilation. Adequate jaw relaxation, a laryngoscope blade, and light source are necessary to visualize the glottis. Many chelonians, especially marine turtles, have a fleshy tongue that makes visualization of the glottis difficult. They also have a short trachea and care must be taken not to intubate one bronchus. An adequately sized uncuffed endotracheal tube is recommended. A cuffed endotracheal tube can be used, but care must be taken not to overinflate the cuff and cause damage to the tracheal mucosa.

During anesthesia, respiration and heart rates are recorded regularly. Supportive care depends on preanesthetic clinical and laboratory findings, the size of the chelonian, and the procedure to be performed. Fluid therapy is accurately administered, even to small chelonians, with a syringe pump; most require maintenance fluid administration of a balanced electrolyte solution at 5 to 10 ml/kg per hour. The patient is kept within the preferred optimal body temperature range for the particular species. During anesthetic maintenance the patient is also evaluated for signs of pain (tachycardia, tachypnea, limb and jaw movement), and the depth adjusted or additional analgesia provided. The anesthetic plane is frequently assessed for the presence or absence of reflexes such as righting, palpebral, cloacal, and limb and tail withdrawal reflexes. At a surgical plane the righting and palpebral reflexes are usually absent. Absence of the corneal reflex and no response to a surgical stimulus indicates a deep plane of anesthesia.

MONITORING

An ultrasonic Doppler flow device is most useful for constantly monitoring heart rate and rhythm. The probe is positioned over the carotid or coccygeal arteries. Alternatively, a pencil probe is placed at the level of the thoracic inlet, close to the heart and major vessels.

Electrocardiography (ECG) is performed with leads attached in a conventional manner and detects changes in heart rate such as tachycardia, bradycardia and arrhythmias. However, it does not evaluate mechanical performance of the heart (Murray, 2006b). Alternately, an esophageal probe is placed, especially in larger chelonians. Electrocardiographic changes following induction of anesthesia require assessment of anesthetic depth, oxygenation, and if necessary adjustment of anesthetic concentrations. Direct arterial blood pressure measurements are most accurate to continuously record arterial blood pressure. Information on normal arterial pressures in awake and anesthetized chelonians is scant and no reference values have been established. Direct arterial blood pressure measurements are impractical in most chelonians because of the limited access to a peripheral artery. A cut-down procedure is required to gain access to the femoral or carotid artery, the latter being the most easily accessible (Dennis and Heard, 2002).

At a surgical plane of anesthesia, chelonians exhibit respiratory depression, especially when placed in dorsal recumbency. Intermittent positive pressure ventilation (IPPV), either manually or via mechanical ventilators, is provided throughout anesthesia and into the recovery period. Ventilators suitable for even small chelonians are available and are ideally suited to provide accurate and constant respiratory support. In most chelonians, the rate of IPPV is usually between 4 and 8 breaths per minute.

The use of pulse oximeters in chelonians to monitor heart rate, arterial oxygen saturation (SpO_2), and diagnose hypoxemia during anesthesia is of limited value because all devices are calibrated based on the human oxygen hemoglobin dissociation curve. In green iguanas there were no significant differences between pulse oximeter readings and arterial blood gas analysis (Diethelm, 2001). However, at present, pulse oximetry in chelonians may be more useful to detect trends in arterial oxygen desaturation. A suitable sampling site is often difficult to locate for both transmission and reflectance probes. In most, an esophageal probe placed at the level of the carotid artery as well as rectal probes can be used.

Arterial blood gas analysis is usually impractical in chelonians because a cut-down procedure is required in most to access the carotid or femoral artery. Blood samples obtained via cardiocentesis are inaccurate because of the mixture of arterial and venous blood within the ventricle.

Although analyzers with low sampling rates (less than 50 ml/min) are available, end-tidal $\rm CO_2$ monitoring in chelonians is inaccurate owing to the presence of cardiac shunts. This is supported by a study in green iguanas that concluded that there is no correlation between end-tidal $\rm CO_2$ concentrations and arterial $\rm PCO_2$ values (Hernandez-Divers, Schumacher, and Hernandez-Divers, 2004). Changes in end-tidal $\rm CO_2$ concentrations may indicate airway leaks or airway obstruction.

RECOVERY

All chelonians are recovered within a temperature and humidity range that meets the natural requirements of the species. For most, small animal incubators are used, and most commercially available incubators offer the ability to provide an oxygen-enriched environment. Heart rate as well as respiratory rate and pattern are regularly monitored and recorded throughout the recovery period. Most chelonians require respiratory support well into the recovery period and positive pressure ventilation with room air should be provided until the patient is breathing spontaneously. Low oxygen concentrations provide the stimulus to breath and high oxygen concentrations in the inspired air may prolong return to spontaneous respiration (Diethelm, 2001). However, some patients especially chelonians with respiratory tract disease may require supplemental oxygen during the recovery period. Oxygen can be administered via facemask at a flow rate of 2 to 5 L/minute depending on the size of the patient, or alternately insufflation with oxygen can be achieved with a nasal catheter, which can be glued or taped to the scales of the head. For long-term nasal insufflation, oxygen should be delivered through a humidifier to prevent drying of the upper and lower airways.

Throughout the recovery period, the level of sedation is evaluated by the absence or presence of the palpebral corneal foot and tail reflexes as well as cloacal tone. If venous access has been established, fluid therapy with a balanced electrolyte solution should be continued, especially in chelonians presented with prior fluid deficits. The author does not recommend an increase in environmental temperature over the species-specific temperature range in order to shorten recovery time, since the increased demand of oxygen by the tissues may not be met in a patient with compromised respiratory function. The patient should be extubated when oral and pharyngeal reflexes have returned and the animal is breathing spontaneously. Only fully recovered animals are returned to their enclosure, especially aquatic species to prevent accidental drowning. Post-operatively, all chelonians recovering from surgical procedures should be re-evaluated for signs of discomfort and pain and the requirement for additional analgesia.

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Cagebirds

Michelle G. Hawkins and Peter J. Pascoe

INTRODUCTION

Growing interest and expertise since the 1960s has resulted in a dramatic increase in the need for safe anesthesia for more specialized medical and surgical procedures. In some circumstances, short anesthetic periods are safer and impose less physiological compromise and stress than physical restraint. Even though differences exist between birds and mammals, the basic principles of anesthesiology apply.

ANATOMICAL AND PHYSIOLOGICAL CONSIDERATIONS

Respiratory

Avian anesthesia presents many challenges owing to the complex structure and function of the respiratory system. An understanding of this unique system is essential in evaluating anesthetic risks and complications. Unlike mammals, the avian respiratory system has separate ventilatory and gas exchange compartments, making it highly efficient compared with other vertebrates (James et al., 1976).

The ventilatory compartment includes the major airways, air sac system, and thoracic skeleton and associated muscles. The epiglottis is absent. When the beak is closed, the choanal slit on the dorsal palate covers the glottis. This allows air flow through the nares to be directed into the trachea. In most species, the glottis is easily visualized at the base of the tongue, making endotracheal intubation straightforward. Although the tracheal rings are complete, they can collapse during physical restraint, especially in smaller birds.

Male ruddy ducks and both sexes of emus have a tracheal sac-like diverticulum that when expanded may be confused with a ruptured trachea (King, 1989). In the emu, it arises as a slit-like opening through incomplete tracheal rings on the ventral surface of the caudal one-fourth of the extrathoracic trachea. The caudal end may

extend almost to the sternum (King, 1989). This sac allows for the booming call of the emu. In the ruddy duck, a pear-shaped sac opens from the dorsal tracheal wall just caudal to the larynx and extends between the esophagus and trachea (King, 1989). This sac is only found in males and may be involved in the billdrumming display. In both species, positive pressure ventilation will inflate the sac and some anesthetic gas may be sequestered, potentially affecting depth. A bandage can be wrapped around the neck to prevent sac inflation. A bullous tracheal enlargement is found in some Anseriformes species (King, 1989). A median septum is present in the trachea of some penguins and petrels. Depending on the species this septum divides the trachea from the bronchial bifurcation cranially for variable distances. For example, in the rockhopper penguin the median septum is only 5 mm in length (King, 1989), but still may allow unilateral endobronchial intubation. In the jackass penguin the median septum extends to within a few centimeters of the larynx, allowing both unilateral endobronchial intubation and the potential for trauma during intubation (King, 1989).

There is also significant variation in tracheal length with important implications for anatomical dead space. The typical bird trachea is reported to be $2.7 \times longer$ than that of a similarly sized mammal. However, because it is approximately 1.3 times wider the net effect on air flow resistance is similar to mammals (King, 1989). Tracheal dead space volume is approximately 4 times that of comparably sized mammals (King, 1989). In some species (e.g., swans, cranes, spoonbills, and cassowarys), convoluted loops and coils further increase dead space. Healthy conscious birds compensate for this larger dead space with a larger tidal volume and lower respiratory frequency than mammals. This results in minute ventilation rates about 1.5 to 1.9 times that of mammals (Powell and Whittow, 2000; Frappell et al., 2001). However, anesthetic drugs depress ventilation and a greater percentage of minute ventilation becomes

dead space ventilation (Ludders and Matthews, 1996; Ludders, 1998).

In most caged birds, four paired (cervical, cranial thoracic, caudal thoracic, and abdominal) air sacs and one unpaired interclavicular extend throughout the coelomic cavity (Duncker, 1971; Duncker, 1972; McLelland, 1989; Jaensch et al., 2002). In addition, diverticula may pneumatize vertebral ribs, sternum, humerus, pelvis, femur, and the cervical and some thoracic vertebrae (Duncker, 1971; Duncker, 1972; Duncker, 1974; James et al., 1976; McLelland, 1989; Jaensch et al., 2002). The air sac membranes are poorly vascularized and do not significantly participate in gas exchange. Instead they function as a mechanical bellows providing tidal airflow to the lungs during ventilation (Duncker, 1971; Duncker, 1974; Magnussen et al., 1976; Scheid, 1979). The thoracic and abdominal cavities are not separated by a muscular diaphragm. Therefore, differing pressures do not occur between the cavities (Duncker, 1974; McLelland, 1989; Scheid and Piiper, 1989). Inspiration and expiration occur through movement of the sternum by contraction of the cervical, thoracic, and abdominal muscles (Duncker, 1971; Scheid and Piiper, 1987). Since both inspiration and expiration require muscle activity, anything that depresses muscle function or impairs thoracic movement decreases ventilation. The degree of drug-induced muscle relaxation depends on the anesthetic(s) used, anesthetic depth, and physical condition of the patient (Ludders, 2001).

Restriction of movement of the sternum and thoracic muscles owing to over-exuberant physical restraint, and dorsal and ventral recumbency are often reported to lead to hypoventilation (King and Payne, 1964; Heard, 1997; Curro, 1998; Forbes, 1999; Jaensch et al., 2002; Pettifer et al., 2002). It has been hypothesized that in dorsally recumbent patients the air sacs and ostia (openings to the lungs) are compressed by the internal organs, an effect exacerbated by increasing anesthetic duration (King and Payne, 1962, 1964). This hypothesis has led to the recommendation to avoid dorsal recumbency in anesthetized birds when possible. However, the only studies of this effect until recently have been in the chicken. The chicken has a very welldeveloped pectoral musculature that may compress the thorax during respiration in dorsal recumbency more so than lighter-bodied birds. Chickens and other domestic poultry also usually have large amounts of intracoelomic fat that reduces air sac volume and adds to the weight of tissues compressing the lungs. Additionally, chickens have a somewhat different gas exchange anatomy that may affect ventilation in dorsal recumbency. Although the chicken is not the most appropriate model, the recommendation for avoiding dorsal recumbency in cagebirds is also supported by clinical experience (King and Payne, 1964; Curro, 1998). In redtailed hawks no significant differences were found in arterial blood gas tensions or pressures when birds were placed in either dorsal or lateral recumbency. However, there was a significant difference in end-tidal ${\rm CO_2}$ between the two positions (Malka, Hawkins, Pascoe, unpublished data). However, any adverse effect of positioning appears to be negated by assisted ventilation.

The parabronchial lungs are the primary site for gas exchange (Scheid and Piiper, 1970; Duncker, 1971, 1972; Barnas et al., 1991). The paired lungs are firmly attached to the ribs and vertebral column dorsally and extend from the thoracic inlet caudally to the adrenals and cranial kidneys (Duncker, 1971, 1972). Avian lungs are relatively small compared with mammalian and the parabronchi are non-expandable. There are two types of parabronchial tissue, and the ratio of these tissues varies with species. The paleopulmonic parabronchial tissue is found in all, comprises the majority of the lung volume in most species, and air flow is unidirectional throughout the respiratory cycle (Duncker, 1971, 1972; McLelland, 1989). Penguins and emu have only paleopulmonic parabronchi. The neopulmonic parabronchial tissue is also found in most species. However, it is only well developed in poultry and songbirds, accounting for approximately 20% to 25% of total lung volume (Duncker, 1972; Fedde, 1980). Air flow through the neopulmonic parabronchi is bi-directional (Duncker, 1971, 1972; McLelland, 1989). Two complete cycles of inspiration and expiration are necessary to completely exchange the inhaled gas (Scheid and Piiper, 1970; Scheid and Piiper, 1989). Most air from the first inspiration is directed to the caudal air sacs. That gas flows from the caudal air sacs into the lungs on the first expiration through a unique system of aerodynamic valves (Banzett et al., 1987; Powell and Scheid, 1989). Air from the lungs moves into the cranial air sacs with the second inspiration and is moved out through the trachea into the environment on the second expiration. This two-breath cycle allows a continuous flow of air to the gas exchange surfaces, whereas the less efficient mammalian breathing cycle allows gas exchange to occur only at the end of inspiration. Owing to this unique system of air flow, a bird with an upper respiratory obstruction can still be ventilated effectively if an air sac is cannulated through the body wall (Piiper et al., 1970; Whittow and Ossorio, 1970; Rode et al., 1990; Wijnberg et al., 1991; Korbel et al., 1994, 1996; Mitchell et al., 1999).

Gas exchange is extremely efficient and a cross current model is used to describe the blood and gas association (Scheid and Piiper, 1970, 1987; Duncker, 1972; Scheid, 1979; McLelland, 1989; Powell and Whittow, 2000). As the gas flow through the majority of parabronchi (i.e., the paleopulmonic parabronchi) is unidirectional, the cross current anatomy of the pulmonary vasculature allows for the continuous exchange of gases throughout the length of the parabronchi. This results in a more efficient oxygen and carbon dioxide exchange than in the mammalian alveolus (King and Payne, 1964; Gleeson and Molony, 1989; Powell and Whittow, 2000). In addition, birds have a larger relative

gas exchange surface area, longer capillary blood transit times, and thinner blood-gas barrier than mammals of comparable weights, resulting in greater gas exchange efficiency (Gleeson and Molony, 1989; McLelland, 1989; Powell and Scheid, 1989; Powell and Whittow, 2000).

Allometric analyses have been used to predict the effect of body size on respiratory variables associated with gas exchange efficiency between mammals and birds (Frappell et al., 1992; Maloney and Dawson, 1994; Frappell et al., 2001). A recent study of 50 species found general agreement with the older allometric equations, with some minor differences in coefficients. The variables determined in this study agree with anatomical data and clinical observations, suggesting that irrespective of body size, birds tend to breathe slower and deeper, have lower minute ventilation, and have a greater demand for oxygen when compared with mammals, making the avian respiratory system more highly efficient in terms of oxygen extraction (Table 22.1).

In mammals, the functional residual capacity (FRC) acts to buffer changes in oxygen partial pressures during the respiratory cycle. In the past, it has been suggested there is little FRC in avian lungs; therefore, birds have little ability to blunt the effects of apnea on PaO₂ and PaCO₂ (McLelland, 1989). However, there is a significant reservoir of gas in the air sacs, and unidirectional flow of gases through the avian lung may minimize the potential for significant fluctuations in blood gas tensions during short periods of apnea. For example, in chickens 8 minutes of apnea after breathing 100% oxygen resulted in blood oxygen tensions that declined at a similar rate to that in mammals (Pascoe, unpublished observations). Having a high concentration gradient (greater than or equal to 95% O₂) and small distances to traverse allows for diffusion of oxygen through the lungs as the oxygen is being removed by the blood, accounting for this delayed onset of hypoxemia. In a bird breathing room air there is a very small diffusion gradient and because oxygen consumption is higher in birds than mammals any periods of apnea, however brief, must be treated immediately.

Avian ventilation is controlled both centrally and peripherally. Respiration rates are lower, in some cases one-third of the mammalian rate for a comparably sized animal (Scheid and Piiper, 1989; Powell and Whittow, 2000). The anatomical location of the central ventilatory controls appears to be in the pons and medulla oblongata,

Table 22.1. Comparison of allometric equations for respiratory variables in birds and mammals (Frappell et al., 2001).

Variable	Birds	Mammals
Oxygen consumption (VO ₂)	16.3 M ^{0.68}	12.9 M ^{0.73}
Minute ventilation (VE)	385 M ^{0.72}	518 M ^{0.74}
Tidal volume (VT)	22.9 M ^{1.08}	10.8 M ^{1.01}
Breaths per minute (f)	17 M ^{-0.34}	49.1 M ^{-0.26}

M = body mass

as in mammals, with facilitation and inhibition most likely coming from higher regions of the brain (Powell and Whittow, 2000). Peripheral extrapulmonary chemoreceptors, specifically the carotid bodies, respond to changes in PO₂ and PCO₂ in the same manner as those observed in mammals (Scheid and Piiper, 1989). The chemical drive on respiratory frequency and ventilatory duration also appears to depend on vagal afferent feedback from intrapulmonary receptors as well as extrapulmonary chemoreceptors, mechanoreceptors, and thermoreceptors (Scheid et al., 1978; Crank et al., 1980; Scheid and Piiper, 1989; Powell and Whittow, 2000).

Birds have a unique group of peripheral receptors, the intrapulmonary chemoreceptors (IPC). They are present in the lung and are exquisitely sensitive CO₂ receptors (Burger et al., 1974; Banzett and Burger, 1977; Scheid et al., 1978; Crank et al., 1980; McLelland, 1989; Powell and Scheid, 1989; Scheid and Piiper, 1989). The rate of action potential generation by IPCs is inversely proportional to PCO₂ as they are inhibited by increases in PCO₂. However, it is unclear whether low lung PCO₂ or high pH is the immediate stimulus for signal transduction in the IPCs (Bebout and Hempleman, 1999). Compared with mammals, respiratory function in birds may be more sensitive to the effects of inhalant anesthetics because of their effect on the avian IPCs, depressing their ability to adjust ventilation in response to PCO₂ changes (Ludders, 2001). Inhalants depress the responsiveness of a number of peripheral control mechanisms that can directly or indirectly affect ventilation (Molony, 1974; Bagshaw and Cox, 1986; Pizarro et al., 1990).

Cardiovascular System

The cardiovascular system also exhibits adaptations to the high metabolic demands of flight. Birds have a proportionally larger heart, higher stroke volumes, cardiac output, and resting mean arterial pressures compared with mammals (Grubb, 1983; Smith et al., 2000). Heart rates vary significantly among species, with resting rates ranging from 150 to 1,000 bpm. Such high rates make obtaining accurate heart rates difficult and very few commercially available monitors are able to count more than 250 bpm.

The Purkinje fibers within the ventricular myocardium completely penetrate the endocardium through to the epicardium, facilitating synchronous beating at rapid heart rates (Keene and Flammer, 1991). This fiber distribution is responsible for the QRS morphology of the avian ECG (Smith et al., 2000). The ventricles and atria receive a higher density of both sympathetic and parasympathetic nerve fibers (Smith et al., 2000).

Endogenous catecholamines are released during stress and pain. They can have a significant impact during anesthesia because some inhalant anesthetics sensitize the myocardium to catecholamine-induced arrhythmias (Greenlees et al., 1990; Aguilar et al., 1995; Ludders and Matthews, 1996). Clinical observations

suggest that manipulation of fractured bones, especially the pectoral girdle, causes significant bradycardia and arrhythmias in some patients. However, it is unknown whether this is a vagotonic or baroreceptor effect. Hypercapnia, hypoxemia, and some anesthetics depress cardiovascular function.

The renal portal system is an arrangement of smooth muscles that form a valve within the external iliac vein at its junction with the efferent renal vein (King and McLelland, 1984). This valve is controlled by both adrenergic and cholinergic stimulation. Epinephrine causes it to relax directing venous blood to the systemic circulation. Acetylcholine contracts the valve, allowing blood from the legs to perfuse the renal tubules (Akester, 1967; Akester and Mann, 1969; Johnson, 1979; Burrows et al., 1983; Palmore and Ackerman, 1985). The clinical significance of the renal portal system is controversial. It may be important where consistent blood levels of a drug (e.g., antimicrobial) are required (Ludders and Matthews, 1996). In ostriches administered xylazine/tiletamine/ zolazepam there was no significant difference between injection in the thigh or muscles at the base of the wings in onset, duration, or recovery (Carvalho, 2006). Until additional studies are performed, the authors recommend that nephrotoxic drugs or drugs exhibiting high renal excretion be administered into the cranial half of the body.

Thermoregulation

Heat is lost via radiation, evaporation, convection, and conduction. The normal body temperature of most caged birds is within 39°C to 43°C (Dawson and Whittow, 2000). Since most are small and have a high surface area to body mass ratio, they radiate heat rapidly. Once anesthetized, the bird is immobile and relaxed so it will generate less heat from muscle contraction. It is also subject to evaporative loss from the respiratory tract (dry anesthetic gases), skin surfaces (surgical preparations solutions) and open body cavities, conduction of heat via surface contact, and convection of warm gases from around the body (Wessel et al., 1966). Anesthesia redistributes blood flow and depresses thermoregulatory response, further promoting heat loss. In pigeons with no external heat support the core body temperature dropped less than or equal to 8°C after greater than or equal to 30 minutes of inhalant anesthesia (Harrison et al., 1985; Jenkins, 1988; Harrison, 1991). Hypothermia has a number of adverse physiological effects; ventilatory depression results in bradypnea, and decreased minute ventilation and tidal volume (Moon and Ilkiw, 1993). In hypothermic mammals decreased receptor response and catecholamine release induce bradycardia and arrhythmias (Weiss et al., 1998). Hypothermia also decreases anesthetic requirement and metabolism, and prolongs recovery (Ludders and Matthews, 1996). Therefore, monitoring of core body temperature and providing thermal support are essential to reduce anesthetic morbidity and mortality in the anesthetized patient.

EQUIPMENT

Endotracheal Intubation

Endotracheal intubation provides a patent airway, reduces dead space, and facilitates positive pressure ventilation. Its disadvantages include tracheal mucosal trauma, increased airway resistance, and airway occlusion because of mechanical forces or secretions. Increased resistance is of greater importance in very small patients because it is inversely related to the fourth power of the tracheal radius. For example, decreasing the radius from 5 mm to 3 mm increases resistance 7 times; whereas decreasing it from 3 mm to 1 mm increases it more than 80 times. Since increased resistance increases the work of breathing, it is minimized by positive pressure ventilation.

Despite these potential adverse effects, intubation is recommended for any procedure greater than or equal to 10 minutes. Many types of endotracheal tubes have been used, including Cole, non-cuffed, and cuffed (Figure 22.1). Cole tubes have a narrow tip that after a short distance flares into an increased diameter. The distal end is advanced into the trachea until the larger diameter abuts the glottis to create a seal.

Over-inflation of cuffed endotracheal tubes causes tracheal mucosal trauma resulting, in part, from lack of expansion of the complete tracheal rings. However, uninflated tubes also cause damage owing to the irregularity of the plastic cuff surface. Additionally, the mucosa appears very susceptible to rubbing injury from the tube tip. Care must be taken to minimize head and neck movement in the intubated patient. Other factors that predispose to mucosal injury include ventilation technique and the endotracheal tube disinfection protocol. Inflammation of the tracheal epithelium may lead to fibrotic narrowing and formation of a trans-tracheal membrane (Figure 22.2). Stenosis and membrane



Figure 22.1. Endotracheal intubation in most birds is straightforward and visualization of the glottis is not difficult.



Figure 22.2. Transtracheal membrane occluding approximately 75% of the tracheal lumen in a double yellow-headed Amazon parrot. Note the significant vascularization of the membrane. These membranes have been reported most commonly in birds up to several weeks after intubation with both cuffed and non-cuffed endotracheal tubes. Various factors such as over-inflation of the cuff, ventilation techniques, and endotracheal tube disinfection protocols have been implicated.

formation require time, and clinical signs (e.g., dyspnea and increased inspiratory effort) may not be evident for several weeks after anesthesia.

Although commonly used, there are several disadvantages to the use of non-cuffed tubes. The inability to provide a sealed airway allows escape of anesthetic gases increasing the amount required, as well as environmental contamination. Also, airway protection from aspiration of secretions or GI contents is reduced. This makes it imperative that the oral cavity be clean prior to intubation and monitored throughout the procedure. Head and neck elevation may reduce regurgitation or reflux of contents from the crop, proventriculus, or ventriculus. Cuffed tubes have been used in larger patients. The cuff is carefully inflated with just enough air to prevent leakage when 10 to 15 cm $\rm H_2O$ pressure is applied to the rebreathing bag (Ludders and Matthews, 1996; Curro, 1998).

The patient size determines the endotracheal tube used. The smallest commercial non-cuffed tubes have an internal diameter (ID) of 1 mm. However, tubes less than 2 mm ID are often highly flexible and kink easily. The smallest diameter cuffed tube is 3 mm ID. Very small birds may be intubated with Teflon IV, red rubber, or urinary catheters. Care is taken to ensure that no sharp edges are present at the end. This can be achieved by using a small piece of silicone tubing over the end of the catheter.

As stated, endotracheal tubes with small internal diameters impose significant resistance to gas flow, especially if mucus accumulates. During inhalant anesthesia, copious thick mucus production can occur owing to

the drying effects of the inspired cold, dry gases. In the authors' experience, humidification of the gases reduces mucus plug formation. Commercially available endotracheal tube humidifiers are available (Humidi-vent Mini Agibeck Product, Hudson RCI, Temecula, CA). Disadvantages of their use include increased dead space and filter plugging with secretions. The use of an endotracheal tube with a Murphy eye, which has both side and end openings, decreases mucus occlusion.

Endotracheal tube obstruction is detected by monitoring the ventilatory pattern. As the airway occludes, expiratory phase duration becomes prolonged (Ludders and Matthews, 1996). An anticholinergic (atropine, glycopyrrolate) reduces mucus production and plug formation. However, it also increases mucus viscosity, making it harder to clear secretions from the tube. Some clinicians recommend for long procedures the endotracheal tube is removed and replaced after every hour.

Extension of the neck, gentle traction on the tongue, and pressure under the mandibular beak will push the glottis forward to aid in endotracheal tube placement. Psittacines have a thick, fleshy tongue that makes glottal visualization slightly more difficult. Some birds have very brisk glottal closure reflexes. Intubation in these patients is facilitated by applying a very small amount of lidocaine to the larynx and waiting 60 seconds. If possible, the tube is secured to the mandibular beak to allow monitoring of the oral cavity during anesthesia. The portion of the tube extending from the breathing system to the glottis is dead space; cutting the tube as close as possible to the oral cavity minimizes this mechanical dead space.

Inhalant anesthetics can also be administered through a cannula inserted into an air sac for induction and maintenance in birds as small as zebra finches (Figure 22.3) (Piiper et al., 1970; Whittow and Ossorio, 1970; Rode et al., 1990; Wijnberg et al., 1991; Korbel et al., 1994; Mitchell et al., 1999; Nilson et al., 2005). Air sac cannulation was first described by Whittow and Ossorio in 1970. It provides an airway when upper respiratory tract obstruction (e.g., syringeal foreign bodies or granulomas) is present. It is also used for procedures involving the upper airway or cranium (Piiper et al., 1970; Jaensch et al., 2001; Nilson et al., 2005). Air sac cannulas are placed for acute life-threatening obstruction and longer-term respiratory support (Korbel et al., 1996; Mitchell et al., 1999).

Tubes used for air sac cannulas include sterile endotracheal tubes, large-gauge IV catheters (16–18 g), red rubber feeding tubes, and silastic tubing. For the bird to breathe through the cannula, the tube diameter should be at least equal to the patient's tracheal diameter. It should also be short enough to minimize dead space and prevent coelomic soft-tissue injury.

Air sac cannulas are usually placed in the left caudal thoracic or abdominal air sac to prevent trauma to the larger right liver lobe. However, placement in the







Figure 22.3. Placement of an air sac cannula. **A.** Strict asepsis should be observed when placing the cannula. Feathers over the site for cannulation should be gently plucked, contour feathers should be taped away from the cannula site, and the area should be surgically prepared. The landmarks for air sac cannula placement are caudal to the last rib, ventral to the vertebrae and, in most cases, cranial to the hind limb. **B.** Once the cannula has been surgically placed, it is secured in place with suture. **C.** A piece of sterile gauze can be used as a filter to minimize contamination of the cannula with particulate matter.

clavicular air sacs has also been reported (Rode et al., 1990). In sulfur-crested cockatoos (*Cacatua galerita*) caudal thoracic air sac intubation provided stable isoflurane anesthesia without significant respiratory functional changes. Even though caudal thoracic air sac PCO_2 decreased to 12.7 ± 7.9 mmHg, spontaneous respiration was still present (Jaensch et al., 2001). Clavicular air sac catheterization was also evaluated, but was not successful at either maintaining anesthesia or providing ventilation. In a separate study, clavicular air sac PO_2 and PCO_2 were significantly lower than in the cranial thoracic air sacs, suggesting, at least in sulfur-crested cockatoos, that ventilation of this air sac is less than the cranial and caudal thoracic air sacs (Jaensch et al., 2002).

Air sac cannula placement is a relatively simple surgical procedure (Figure 22.3). A skin incision is made over the desired site. The underlying muscle and air sac membrane are bluntly dissected with a hemostat. The tip of the sterile catheter is grasped with the hemostat and passed into the air sac. The muscle and skin are closed securing the catheter in place. In an emergency, gas flow and ventilation are provided through an IV catheter placed at the same site and connected to an oxygen source. Care is taken not to advance the catheter too far and limit oxygen flow to prevent hypocapnia. In 1 to 1.7 kg chickens a flow of 500 mL/min reduced PCO₂ to greater than or equal to 20 mmHg (Pascoe, unpublished observations). Oxygen and anesthetic gases from the cannulated site exit the trachea unless intubated with an occluded endotracheal tube. It is possible to scavenge waste gases by placing a mask or tube over the bird's head and connecting it to an active anesthetic scavenging system.

The most common adverse effects reported with air sac cannulation are apnea, subcutaneous emphysema, plugging of the tube, and bacterial contamination with associated coelomitis (Mitchell et al., 1999; Jaensch et al., 2001). Ensure meticulous cleaning and inspection of the tube to prevent plugging. Cleaning is performed with a sterile cotton-tip applicator or Dacron swab. A filter is designed from small-weave gauze and placed over the end of the tube to prevent particulate matter from entering. Although most birds tolerate air sac cannulas, an Elizabethan collar may be required in some. An air sac cannula is left in place for 3 to 5 days; the body wall is closed after removal to prevent subcutaneous emphysema.

Breathing Systems

Many non-rebreathing systems (e.g., Ayre's T-piece, Mapleson systems, Magill, Jackson-Rees, Norman elbow, and Bain) can be used. These systems require a relatively high fresh gas flow rate to remove carbon dioxide. These higher flow rates have the added benefit of providing rapid equilibration in inhalant concentration with changes in vaporizer setting. Non-rebreathing systems were traditionally viewed as ideal for small

patients because of lower airflow resistance and reduced dead space. Circle systems were believed to have higher airflow resistance because they contain one-way valves and soda lime canisters. However, the primary source of resistance is most likely the endotracheal tube. Recent studies in infants less than or equal to 10 kg (Rasch et al., 1988) and cats (Suter et al., 1999) have shown that resistance was insignificant compared with that produced by the endotracheal tube alone. Circle systems are heavier and bulkier, which predisposes to accidental extubation and difficulty working around the head. For this reason, the Bain breathing system is recommended in small birds because of its lightweight design.

Specific flow rates have not been defined. As in mammals, 2 to 3 times minute ventilation appears appropriate when using the T-piece or Norman elbow, but in the Bain circuit a lower flow rate of 150 to 200 ml/kg per minute is effective (Ludders and Matthews, 1996; Ludders, 2001). The removal of waste gases from the circuit occurs during the pause between expiration and inspiration. If the respiratory rate is high (shorter pause and therefore more mixing of inspired and expired gases) a higher flow rate is used (e.g., RR greater than 40 increase the flow rate to 300 ml/kg per minute).

Ventilators

Ventilators must cope with the range of tidal volumes in the species of interest. In very small birds this may be less than or equal to 1 ml, whereas in a large ostrich it might be greater than or equal to 2 L. Modern ventilators are usually pneumatic, but control mechanisms may be either pneumatic or electric. If electronically controlled, an auxiliary power source is required if the bird is moved or power fails. The three variables controlled by a ventilator are tidal volume, rate of tidal volume delivery, and respiratory frequency. The method of control varies among ventilators.

In volume-limited ventilators, tidal volume is set with the expectation it will deliver the volume regardless of moderate changes in resistance. Even if the circuit is disconnected the ventilator continues to cycle with no alteration in tidal volume or timing. Some ventilators allow the upper limit for inspired pressure to be set with an alarm.

In pressure-limited ventilators the end-inspiratory pressure is set. The ventilator will push gas into the bird until it reaches the set pressure. The inspiratory phase will then terminate and the ventilator allows passive exhalation. A disconnect or large hole in an air sac is indicated by prolonged inspiration because the preset pressure is not reached.

A third method is to set inspiratory time and achieve different tidal volumes by altering inspiratory flow rate. This is a form of volume-limited ventilation. The respiratory rate and tidal volume are determined by the gas flow. Hence, it is necessary to set a higher flow for a larger tidal volume. On some ventilators this is set by

altering the knob labeled "I:E ratio." This is the inspiratory versus expiratory time and the setting depends on the number of breaths/minute. If you want inspiration to take 1.5 seconds the I:E ratio is set at 1:3 for 10 breaths/minute (6 seconds/breath, 1.5 seconds inspiration:4.5 seconds expiration) or 1:1 for 20 breaths/min (3 seconds/breath 1.5 seconds each for inspiration and expiration). The number of breaths/minute is mostly set by altering a timing device that begins inspiration after a set time period.

In most birds it is essential to have a ventilator that will slowly deliver small tidal volumes to give an acceptable inspiratory time. During anesthesia the ventilator initiates the breath, not the bird, to control PCO_2 . In assisted ventilation the bird initiates the breath when its PCO_2 reaches the point set by the central respiratory controllers. Since the latter are depressed by anesthetics, assisted ventilation is not likely to decrease PCO_2 .

PRE-ANESTHETIC EVALUATION

The medical history and husbandry of the pet bird is essential for pre-anesthetic evaluation. History includes the diet, appetite, previous diseases, and drug therapy. Examination of the cage and its contents is used to assess for heavy metal exposure and the composition of the droppings. The quantity and quality of the latter will determine whether the bird has been eating. Changes in color or consistency suggest GI, hepatic, or urinary system abnormality.

Time is allowed for acclimation to new surroundings to reduce stress and potentially unmask clinical disease. A complete physical examination including respiratory, cardiac, renal, and hepatic function is performed and baseline values recorded for comparison during anesthesia. The bird is examined closely in its cage, paying particular attention to respiratory rate and effort. The resting respiratory rate is recorded prior to physical restraint for comparison with those under anesthesia. The quality of respiration is evaluated by ausculting the air sacs ventrally and the lungs dorsally for evidence of harsh airway sounds or evidence of wheezing. The trachea is also auscultated and gently palpated for abnormalities. The heart is auscultated for murmurs and a baseline heart rate recorded. Pulse quality is assessed at either the brachial or medial metatarsal arteries for symmetry and strength. The body weight is recorded for calculating accurate fluid and medication dosages.

Assessment of renal and hepatic function is difficult. Urine and urates in the droppings are evaluated for quantity and color. Red-tinged urine could be caused by hematuria or dietary colorings. Green or yellow urate discoloration may be biliverdinria and a sign of hepatic dysfunction. Coelomic palpation is performed to assess for organomegaly that may mechanically compress the air sacs and lungs.

Hydration status is evaluated, recorded, and dehydration corrected, if possible, prior to anesthesia. Compensatory mechanisms are blunted under anesthesia, exacerbating underlying hypotension and poor peripheral perfusion. Hydration assessment includes examination of the moistness of the cloacal and ocular mucous membranes and the elasticity of the skin at the eyelids and over the keel. Sunken eyes and cool extremities also suggest dehydration. The refill time after digital compression of the median ulnar vein should be immediate; venous refill times of greater than 1 second have been suggested to correlate with greater than 7% dehydration (Steinhort, 1999). The PCV is often increased during dehydration. In pigeons water deprived for 72 hours, the plasma urea nitrogen increased 6.5 to 15.3 times, but the uric acid only showed a 1.4 to 2 times increase (Lumeij, 1987).

Ideally, a complete blood count and biochemical profile are performed prior to anesthesia. If one hematocrit tube of blood can be collected, a packed cell volume (PCV), whole blood smear for estimated white blood cell count and differential, blood glucose, and several other biochemistry tests can be obtained. There are several new biochemical analysis tabletop systems that only require a very small volume of blood to provide a complete biochemistry profile. Any anemias are characterized as either acute or chronic and regenerative or non-regenerative. Acute anemias are corrected prior to anesthesia as birds may not be able to compensate for lowered levels of oxygen delivery. Transfusion is indicated if the PCV is less than 15% to 20% and the total solids are less than 3 to 3.5 g/dl. However, pet birds often have PCV greater than or equal to 40%, so if the blood loss is acute, the authors may perform a transfusion at a higher PCV. Also, avian total protein values may be much lower than those in mammals (2-3 g/dl). There is a poor correlation between total solids measured by refractometer and protein values measured with the biuret method, making the former an inaccurate criterion for avian transfusion (Lumeij and de Bruijne, 1985). The type of surgery to be performed and potential for blood loss is assessed, so a fluid plan can be prepared. PCV may decrease 3% to 5% during anesthesia owing to vascular hemodynamic changes associated with certain anesthetic drugs. Hypoglycemia (less than 200 mg/dl) is supplemented before anesthesia and glucose concentration monitored closely.

The GI system has a very rapid transit time compared with most mammals. Therefore, it is important to carefully consider the nutritional status of the patient. Prolonged anorexia leads to a negative energy balance requiring nutritional support in the perianesthetic period. Other indications include reduced to absent fecal production and significant reduction in body weight. Nutritional requirements differ among species and classes. To determine the nutritional requirements

for a critically ill patient, the basal metabolic rate (BMR) is first calculated: BMR (kcal/day) = K (BW $_{
m kg}$ ^{0.75}); K = 78 non-passerines; K = 129 passerines. The maintenance energy requirements (MER) are adjustments to the BMR based on hypermetabolism associated with any disease processes. The most common adjustments are 1.2 to $1.5 \times BMR$ (range $0.5-2.0 \times$).

It is difficult to achieve caloric requirements at higher MERs with enteral nutrition. The volume of each feeding is restricted by the patient's size; maximum volume of approximately 0.5% to 1.0% body weight/ feeding is a general rule of thumb. Enteral feeding formulas are also limiting as most provide only 1.0 to 1.5 kcal/ml. Increased feeding frequency is often necessary to achieve calculated requirements. Gavage feeding via the crop is most commonly used. Red rubber tubes or metal feeding needles, with or without mouth speculums, are used, but it is important to ensure the crop is empty before feeding. Complications include regurgitation, aspiration, and esophagitis. Ingluviotomy tubes are used for long-term enteral feeding or when necessary to bypass the oral cavity or proximal esophagus. Pro-ventricular feeding tubes are indicated if upper GI dysfunction is present. However, the proventriculus is thin-walled and easily perforated.

The chosen diet depends on the patient's nutritional needs. Foods can be blended to a liquid, or commercially available enteral products are used based on the patient's protein, carbohydrate, and fat requirements. Total parenteral nutrition or partial enteral nutrition are not commonly used because of catheter-related complications, poor patient tolerance, and lack of appropriate formulations. Calcium gluconate is administered in African grey parrots prior to induction to prevent hypocalcemia, a common problem in these species.

Fasting

Fasting duration is determined by species, size, and clinical status. In birds fasting times are short to reduce regurgitation yet minimize hypoglycemia (Harrison, 1991). Fasting between 2 and 4 hours has been recommended in medium-sized psittacines, whereas birds less than or equal to 100 to 200 g may not be fasted because of high metabolic rates and easily depleted glycogen stores. However, in broiler chickens and adult Japanese quail fasted 12 and 48 hours, respectively, blood glucose remained within clinically acceptable ranges (van der Wal et al., 1999; Lamosova et al., 2004). No studies have been performed evaluating the effect of fasting on psittacines. Scheduling procedures as early in the day as possible reduces fasting times. In species with high metabolic rates, clear fluids high in carbohydrates may be provided to maximize calories while minimizing crop and stomach contents prior to anesthesia. The crop contents may be gently aspirated if anesthesia cannot be delayed.

SUPPORTIVE CARE

Positive Pressure Ventilation

Both injectable and inhalant anesthetics cause dosedependent respiratory depression. Sick or debilitated birds may not be able to accommodate these physiological changes, requiring intermittent positive pressure ventilation (IPPV). In mammals, IPPV is associated with reduced cardiac output and hypotension (Steffey and Howland, 1977; Steffey and Howland, 1980). In cranes anesthetized with isoflurane, spontaneous ventilation was associated with elevations in PaCO₂, hypotension, and acidemia compared with controlled ventilation (Ludders et al., 1989a). There was a significantly reduced PaCO₂-PETCO₂ gradient and no significant difference in mean arterial blood pressure in Hispaniolan parrots (Amazona ventralis) ventilated using IPPV compared with birds breathing spontaneously (Pettifer et al., 2002). It is possible that reduced cardiovascular performance associated with IPPV may not be a concern in birds. However, it is still recommended cardiovascular variables be monitored closely during IPPV.

The authors recommend initial inspiratory pressures of 8 to 10 cm $\rm H_2O$ and rates of 6 to 10 breaths/minute. Thoracic excursions are assessed as soon as the ventilator is started. The tidal volume is adjusted to achieve an appropriate thoracic-abdominal expansion. The minute volume is lower than mammals (Frappell et al., 2001) and inspiratory times can be longer. At 6 breaths/minute the I:E ratio is set at 1:2 to 1:3 (inspiration occurring over 3.3–2.5 seconds). During coelomic surgery, when the air sacs have been opened, anesthetic is pushed into the air being breathed by the surgeons. It is important to avoid or minimize exposure to inhaled agents by personnel. In some cases injectable anesthetics are used if concerns about using inhalant anesthetics are great.

During positive pressure ventilation, it is possible that the direction of gas flow within the lung is reversed. However, the crosscurrent exchange system is not dependent on direction of flow and does not significantly affect gas exchange (Piiper et al., 1970; Ludders et al., 1989a). If a mechanical ventilator is not available, hand ventilation delivered from the reservoir bag provides assisted ventilation.

Fluid Support

Daily maintenance fluid rates are approximately 40 to 60 ml/kg per day. This range is based on studies in which drinking is the main route of water intake. Birds weighing greater than or equal to 100 g drink approximately 5% to 8% of body mass per day. This increases at progressively smaller body masses drinking rates to as high as 50% for birds weighing 10 to 20 g (Bartholomew and Cade, 1963; Zeigler et al., 1972; Skadhauge, 1981). Therefore, it is important to consider the size and

species of the patient before relying on a general range of daily maintenance fluid rates for all birds.

Estimation of fluid replacement is based on body weight and dehydration percentage: Estimated Dehydration (%) \times body weight (g) = fluid deficit (ml). One-fourth to one-half the deficit is given in the first 6 to 12 hours, then the remainder over the following 24 hours (Abou-Madi and Kollias, 1992).

Oral (PO) fluids are only useful for mild dehydration and are contraindicated in head trauma, GI stasis, lateral recumbency, or seizures. Subcutaneous (SC) fluids are commonly used for maintenance and mild-to-moderate dehydration. However, large volumes may not be absorbed because of the paucity of blood vessels in the subcutis and peripheral vasoconstriction. Volumes of 5 to 10 ml/site are injected in the inguinal folds, axilla, or dorsum. Overdistention of the SC site compromises of the blood supply and decrease fluid absorption. Before each injection, the administration site is inspected for previous delays in absorption. Only isotonic or nonirritating fluids are given SC. Dextrose solutions greater than or equal to 2.5% are not given SC, as equilibration between the fluids and the extracellular fluid exacerbate pre-existing electrolyte imbalances (Abou-Madi and Kollias, 1992; Steinhort, 1999).

During anesthesia or emergencies intravenous (IV) or intraosseous (IO) fluids are used to provide replacement fluids. Sites for IV catheters include the basilic (ulnar), medial metatarsal, or jugular veins. Small bore over-the-needle catheters (less than or equal to 24 g) are used. Catheter maintenance is hindered by vessel fragility, lack of dermal tissue, and patient temperament. The site is aseptically prepared and catheters secured with a bandage tape butterfly and suture using an everting mattress pattern to provide a tunnel of skin. Jugular catheters require 24-hour monitoring because fatal hemorrhage can occur if the bird pulls or chews on the catheter and damages the vessel.

Intraosseous catheterization is used in smaller patients or during cardiovascular collapse (Ritchie et al., 1990; Lamberski and Daniel, 1992; Aquilar et al., 1993; Valverde et al., 1993). IO catheter maintenance is easier to achieve owing to stability in the medullary cavity. Products that can be used include 18- to 24-g, 2- to 5-cm spinal needles or 18- to 25-g, 2-cm hypodermic needles. The length of the catheter should be long enough to extend one-third to one-half the length of the medullary cavity. A wire stylet may be necessary with hypodermic needles to reduce the potential for a bone core. Most commonly used sites include the distal ulna and proximal tibiotarsus. Pneumatic bones (i.e., the humerus and femur) are avoided. Feathers are gently plucked and the site surgically prepared (Figure 22.4A). Wearing gloves, the sterile IO catheter is positioned at the center of the cnemial crest of the tibiotarsus or slightly ventral to the dorsal condyle of the distal ulna











Figure 22.4. Intraosseous (IO) catheter placement in the distal ulna of a bird. Strict asepsis should be observed when placing the catheter. Feathers over the site should be gently plucked and the site should be surgically prepared **A.** Wearing sterile gloves, the sterile catheter is positioned slightly ventral to the dorsal condyle of the distal ulna and parallel to the bone. The bone is held firmly with one hand while the hand other applies firm pressure combined with slight rotation **B.** The cannula should be flushed with heparinized saline and should flow easily **C.** The insertion site should be covered with an antibiotic ointment and the cannula should be secured with a bandage tape butterfly at the exit point in the skin and suture **D.** A bandage can be placed over the cannula site for additional security and to prevent possible trauma or damage to the catheter **E.**

and parallel to the bone (Figure 22.4B). The bone is held firmly with one hand while the other applies firm pressure combined with slight rotation. Once the cortex is penetrated, the catheter should advance easily with little resistance. If there is further resistance, the opposite cortex has most likely been penetrated. The cannula is flushed with heparinized saline that should flow easily

(Figure 22.4C). Fluids will be seen flowing through the basilic vein when the cannula is correctly placed in the distal ulna. The insertion site is covered with antibiotic ointment and the cannula secured with a bandage tape butterfly at the exit point in the skin and sutured (Figure 22.4D). A bandage can be placed over the cannula site for additional security to prevent trauma or damage to the catheter (Figure 22.4E). Although IO catheters are reported to remain patent for 72 hours without flushing (Ritchie et al., 1990), it is recommended the catheter be gently flushed with heparinized saline twice daily.

Complications associated with IO catheterization include penetration of both cortices, failure to properly enter the medullary cavity, and extravasation of fluids with associated pain. Extravasation has also been associated with proper catheter placement after 1 to 2 days of use (Steinhort, 1999). Intraosseous catheterization is contraindicated in septic patients and those with metabolic bone disease. Osteomyelitis may occur owing to duration or placement of the IO catheter (Steinhort, 1999). Administration of alkaline or hypertonic solutions may also contribute to osteomyelitis and will cause pain and transient microscopic changes in the bone marrow (Ritchie et al., 1990; Lamberski and Daniel, 1992). Therefore, these solutions are diluted prior to administration and the catheter is flushed with heparinized saline after any drug injection.

Crystalloid fluids such as 0.9% NaCl (Baxter, Deerfield, IL), lactated Ringer's solution (Abbott Laboratories, North Chicago, IL), Normosol-R (CEVA Laboratories, Overland Park, KS) and Plasmalyte-A (Baxter, Deerfield, IL) are commonly used for IV volume support, maintenance and rehydration. Fluids are warmed to body temperature (38°C–39°C) to prevent hypothermia. This warming does not affect composition (Curro, 1998).

In the healthy anesthetized patient replacement fluid rates of 10 ml/kg per hour are recommended. This rate is based on studies in human patients. Although this is a starting point, it is recognized that rates in very small patients may need to be considerably higher. Each patient is assessed individually for fluid needs. Fluid boluses of 10 to 20 ml/kg over 5 to 7 minutes are well tolerated (Abou-Madi and Kollias, 1992). For severe hemorrhage, whole blood transfusion (volume for volume) should be provided. If this is not available, it has been recommended to use crystalloid fluids at 3 times the volume of blood loss. However, this recommendation is based on mammals, in which the interstitial space is 2 times the vascular volume. In birds, the interstitial space is 4 times plasma volume (Skadhauge, 1981). Replacement fluid volumes may need to be greater than 3 times blood loss. Dextrose solutions are added to fluids for treatment of hypoglycemia. Parenteral dextrose use is minimized to prevent compartmental shifts in electrolytes and water leading to hypovolemia (Abou-Madi and Kollias, 1992).

Hypertonic fluids (e.g., 7.5% NaCl) are used to expand intravascular volume during resuscitation following acute severe hemorrhage. In birds hypertonic saline has been used primarily for studying renal sodium excretion and the role of osmotic thirst in the control of normal drinking. In several studies plasma osmolality increased after bolus infusion (Yeomans and Savory, 1988; Leary et al., 1998). The major benefit of hypertonic saline is intravascular volume expansion at one-fourth the volume of isotonic solutions. The mammalian dosage (4 ml/kg) given over 10 minutes is used. However, owing to osmotic diuresis and rapid redistribution of sodium cations the intravascular effect is transient (less than 30 minutes) and additional fluid therapy with a crystalloid or colloid must be used. Hypertonic fluids are contraindicated in dehydration, hypernatremia, and head trauma with intracranial hemorrhage. The sustained use of hypertonic saline is not recommended because hypernatremia and hyperchloremic acidemia, increased bleeding, and exacerbation of underlying cardiac and pulmonary disease resulting from fluid overload may occur.

Small patient size and species diversity often preclude the use of natural colloids such as homologous or heterologous plasma. The indications for the use of synthetic colloids such as hetastarch 6% (Braun Medical Inc., Irvine, CA), Hextend (BioTime Inc., Emeryville, CA), and hemoglobin-based oxygen carriers (Oxyglobin, Biopure, Cambridge, MA) are the same as hypertonic saline, although the benefits last longer. All are cleared through the kidneys so they are used with caution in patients with cardiac or renal impairment. They do not provide albumin, thrombocytes, or coagulation factors. Potential adverse effects include anaphylactoid reactions and blood coagulation abnormalities. In critically ill raptors boluses of hetastarch (10 to 15 ml/kg 6%, q 8 hours) for less than or equal to four treatments were well tolerated (Stone and Redig, 1994). Alternatively dosages less than or equal to 20 ml/kg per day are suggested.

Reported circulating blood volume% based on body weight vary considerably (5% in ring-necked pheasants, $7.5 \pm 1.5\%$ in quail, 16.3%-20.3% in the racing pigeon, $10.6 \pm 2.9\%$ in the galah, and $5.4 \pm 10.5\%$ and $13.1 \pm$ 2.3% in two strains of chickens) (Makinde et al., 1986; Takei and Hatakeyma, 1987; Campbell et al., 1994; Jaensch and Raidal, 1998). Hemorrhage is better tolerated than in mammals. However, when severe (greater than or equal to 30% blood volume) blood loss occurs or the PCV is less than or equal to 20%, whole blood transfusion is indicated. Heterologous blood cells (e.g., from pigeon or chicken) transfused into parrots last only 12 hours, causing a significant metabolic drain on the recipient as the body uses energy to destroy the foreign cells (Sandmeier et al., 1994; Finnegan et al., 1997). The halflife of homologous and autologous blood transfusions were 8.5 and 9.9 days in conures (Aratinga spp.) (Degernes and Crossier, 1999), 12.5 and 12.2 days in



Figure 22.5. Fluid infusion and syringe pumps are commonly required to provide accurate infusion rates in small avian patients.

cockatiels (*Nymphicus hollandicus*) (Degernes et al., 1999b), and 7.1 and 26.8 days in pigeons (Sandmeier et al., 1994), respectively. In pigeons the PCV and total solids were elevated for up to 102 hours following homologous transfusion (Finnegan et al., 1997).

The storage of whole blood or blood products has been little studied (Morrisey et al., 1997), and transfusions with fresh whole blood are recommended. The anticoagulants citrate phosphate dextrose adenine (CPDA-1) and acid citrate dextrose (ACD) are used most commonly at a ratio of 1:9 anticoagulant:whole blood. If given rapidly the citrate can decrease ionized calcium and myocardial contractility. It may be necessary to give calcium gluconate or chloride to reverse this effect. Donors are screened for infectious diseases and a major/minor crossmatch is performed prior to transfusion. In one small study, 66% of major crossmatches performed among different species were positive for agglutination or hemolysis, whereas among the same species they were all negative (Stauber et al., 1996). Mammalian protocols are presently followed for blood collection and administration.

There is little published information on the safety and efficacy of hemoglobin-based oxygen carriers (HBOC). Evaluation of the effects of fluid resuscitation in an acute blood loss (60% blood volume) model in ducks (*Anas platyrhnychos*) showed decreased mortality in birds receiving HBOC combined with crystalloid fluids. The comparison groups received hetastarch combined with crystalloid fluids and crystalloid fluids alone (Lichtenberger et al., 2003). HBOC has a short half-life in mammals (30–40 hours). Adverse effects in mammals include discolored mucous membranes, sclera, and urine affecting patient monitoring (Antinoff, 2003; Lichtenberger, 2004). Rapid bolus infusion (5 ml/kg

HBOC and 10 ml/kg crystalloid fluids over 1 minutes) have been given in patients with acute blood loss without any adverse effects (Lichtenberger et al., 2001, 2002, 2004).

Standard micro-drip fluid sets used in small animal veterinary practice (60 drops/ml) do not allow appropriate infusion rates in very small patients. Instead, fluid infusion and syringe pumps are used for accurate fluid administration (Figure 22.5).

Thermal Support

Body temperature is monitored continuously throughout anesthesia. As discussed, prevention of heat loss is essential and supplemental heat sources are used regardless of procedure length. Electronic thermometers and temperature probes provide accurate readings. Cloacal temperatures have been correlated with thoracic esophageal readings, suggesting that the core temperature may be indirectly monitored (Phalen et al., 1996). However, as cloacal musculature relaxes, peripheral temperature readings are lowered. Esophageal temperature probes provide consistent readings when placed at the level of the heart in the thoracic esophagus. Care is taken to ensure the crop is not damaged during placement and the probe does not back out, resulting in incorrect temperature readings.

Since most heat is lost via radiation, the most effective technique to prevent heat loss is to minimize the temperature gradient between the bird and the room. Options include increased room temperature, insulating the patient with clear plastic drapes, and wrapping non-surgical fields. The surgical time and the amount of time that the body cavities are open are minimized, as are feather plucking and alcohol use for skin preparation. Latex gloves, empty fluid bags, or plastic bottles can be filled with water, warmed in a hot water bath, or microwaved and placed next to the bird. Water bottles are always wrapped in a towel to prevent burns. Circulating warm water blankets insignificantly diminish rate of heat loss in birds (Phalen et al., 1996; Rembert et al., 2001). Radiant heat lamps are effective at maintaining core body temperature, but the optimal distance between the heat source and the patient differs with patient size, heat lamp strength, and heat setting (Phalen et al., 1996; Rembert et al., 2001). Forced air warmers (Bair Hugger, Arizant, Prairie, MN) are more effective at minimizing hypothermia during anesthesia than other methods (Borms et al., 1994; Machon et al., 1999; Rembert et al., 2001). They are particularly effective when set up to have warm air rising around the patient either by wrapping the patient in the blanket or using a perforated table. The patient's eyes are well lubricated to prevent corneal ulceration caused by drying.

Further reductions in heat loss are achieved by warming fluids and reducing respiratory cooling. In pigeons anesthetized for 90 minutes there was no significant difference in heat loss between a circle system with mechanical ventilator producing heated air,

a non-rebreathing system with mechanical ventilator producing non-heated air, and a Bain non-rebreathing circuit (Boedeker, 2005). This is in contrast to humans, cats, and rabbits, in which heated humidified anesthetic gases reduce or prevent the development of hypothermia (Shanks, 1974; Newton, 1975; Tausk et al., 1976; Haskins and Patz, 1980). In intubated anesthetized ringnecked doves (*Streptopelia risoria*) without thermal support, hypothermia was not lessened by humidification and heating of inspired gases (Phalen et al., 1996). However, in anesthetized pigeons maintained on a face mask, heated inspired air did obtund hypothermia (Jenkins, 1988).

Emergencies

Emergencies during anesthesia should be anticipated and planned for in advance. Most are averted by careful monitoring of respiratory and heart rates and body temperature. Emergency equipment (i.e., endotracheal tubes, oxygen, IV catheters and materials for securing them, ventilatory support, and emergency drugs) must be close by and prepared for use. It is recommended that emergency drug dosages be calculated and the doses predrawn before induction (Table 22.2). Respiratory depression and arrest are treated by turning off the anesthetic and controlling ventilation. Cardiac arrest is usually a result of myocardial hypoxemia and inotropic and chronotropic anesthetic drug effects. Although treatment is often unrewarding, administration of epinephrine (IV, intrapulmonary, or intracardiac) is recommended. Cardiac massage is nearly impossible because of the heart's anatomical location dorsal to the large bony sternum. Severe bradycardia is treated with atropine, assuming it is owing to increased parasympathetic tone. In very small birds, it is possible to see spontaneous ventricular defibrillation, as the mass of the heart is small enough that it cannot maintain a fibrillatory pattern.

RESTRAINT

Correct restraint is essential to minimize stress and time to anesthetic induction. Stressed birds may die from restraint, a risk magnified in sick or debilitated patients. Physical restraint must be assessed for each patient and appropriate stabilization and supportive care preplaced prior to handling. Paper towels, wash cloths, hand towels, large bath towels, or blankets are used based on the patient size. Leather gloves will not protect from the crushing bite of a large parrot. Nets are used to capture birds in larger enclosures or escapees. They are sized appropriately for the patient to minimize iatrogenic trauma. Once netted, the bird is gently removed to avoid trauma to the wings, legs, or toes. Ear protection for the handler (e.g., cotton balls or ear plugs) can be used when handling large psittacines (e.g., cockatoos and macaws). Face shields or goggles are used when handling birds likely to inflict ocular damage with the tip of their beaks (e.g., Ciconiiformes).

For capture the patient is confined to the smallest area that will allow for safe and rapid restraint. Ideally the room is free of windows and doors leading to the outdoors. Alternately, windows are covered to minimize self-trauma if an escape occurs and doors are locked. If the bird must be captured within the room it is placed on the floor in a corner to restrict movement. The bird is never captured from the hand or shoulder of an owner. Turning the lights off decreases excitement in some birds and facilitates capture. Confinement to a travel carrier or hospital cage is preferred for capture. All perches, toys, and food and water dishes are removed to facilitate capture and minimize trauma. Ambient noise is minimized.

Regardless of the technique employed, care must be taken not to compromise thoracic cage movement or the ability of the anesthetist to monitor the patient. Movement with the bird in hand is quiet and calm to reduce fright and stress. The capture is performed expeditiously to minimize stress. If the bird escapes and needs to be recaptured or is unduly excited, delay anesthesia until it has calmed down.

Caged bird capture is performed using a towel, the size of which is dictated by the patient. Capture should be quick, but quiet and gentle to reduce unnecessary stress. The towel is initially placed over the dorsum, and then gently wrapped around the wings to restrict flapping. Birds are removed from the towel if possible to prevent hyperthermia. Small birds (e.g., passerines) are restrained with the head between thumb and forefinger, and the body within the palm. Alternatively, in smaller psittacines the head is restrained using a three-point technique with thumb and middle finger supporting the mandible and the index finger on top of the head. Bruising of the face is possible in large macaws and only the minimum pressure necessary to restrict movement is applied. Gentle extension of the bird's neck further limits

Table 22.2. Emergency drugs used in birds.

Drug	Dosage	Route	Comments
Atropine	0.01-0.02 mg/kg	SC, IM, IV	Most species/ preanesthetic
•	0.04-0.1 mg/kg	SC, IM, IV, IO, IT	Bradycardia
	0.5 mg/kg	IM, IV, IO, IT	CPR
Glycopyrrolate	0.01-0.02 mg/kg	IM, IV	Slower onset than atropine. Most species/preanesthetic
	0.04 mg/kg	IV	Ratites
Epinephrine (1:1000)	0.05-0.5 mg/kg	IM, IV, IO, IT	CPR, bradycardia

head movement. Large parrots are strong and will inflict severe wounds if the head and beak are not immediately controlled. The handler swiftly places the towel over the parrot and immediately immobilizes the bird's head. Some prefer to encircle the bird's neck with their fingers for restraint. A third technique places the thumb under the intermandibular space while the other fingers are placed over the top of the head. This is the author's choice for maintaining full control of the head of larger psittacines during restraint. The other hand is placed on the dorsum to secure the wings and legs.

VASCULAR ACCESS

Sites for IV catheterization include the basilic (ulnar), medial metatarsal, or jugular veins (Figure 22.6). Small bore over-the-needle catheters (less than or equal to 24 g) are used. If blood is to be repetitively collected from the catheter it is placed in either the jugular (small patients) or a large peripheral vessel. Catheter placement and maintenance is hindered by vessel fragility, lack of dermal tissue, and patient temperament. The catheter site is gently plucked and aseptically prepared. Catheters are secured with a bandage tape butterfly and sutured with an everting mattress pattern. The catheter site is bandaged for additional security. Complications of long-term, indwelling catheterization include infection and fatal hemorrhage.

Arterial catheterization for evaluation of blood pressure, blood gas tension, and pH can be performed in many species. They are usually used during anesthesia and removed prior to awakening. The most common sites include the brachial and carotid arteries (Figure 22.7). The catheters are usually placed percutaneously, but a cut-down procedure is sometimes required to confirm arterial location. Significant arteriospasm may occur in some species. Cutaneous application of a small amount of local anesthetic gel (EMLA) 30 minutes prior to percutaneous catheterization may reduce arteriospasm. Alternatively, diluted 2% lidocaine is applied directly over the artery during a cut-down procedure.

ANESTHESIA

Mask or Chamber Induction

Inhalant induction is usually performed with either a mask or induction chamber. Commercially available veterinary inhalant masks can be used for many species. However, differences in beak anatomy and location of nares require unique masks to be formed from syringe cases, plastic soda bottles, or other materials. The mask is as small as possible and the entire head of the patient is placed inside. To minimize waste gas release, a seal is developed using a disposable latex glove placed over the mask with a central hole cut for the bird's neck. Although some have suggested that this seal can be used for positive pressure ventilation, it is not recommended





Figure 22.6. Sites for intravenous (IV) catheters include: **A.** the ulnar (basilic) vein; **B.** the medial metatarsal vein; or the jugular vein. Small bore over-the-needle catheters (24 g or smaller) are most often necessary for avian patients.

by this author. In addition to increased waste gas release, this technique introduces gas into the GI tract.

Face mask induction in some birds (i.e., waterfowl) is associated with apnea and bradycardia that may last for 3 to 5 minutes (see Chapter 24) (Ludders and Matthews, 1996). This response may also occur from placing a face mask snugly onto the face alone. It is a stress response mediated by stimulation of trigeminal nerve receptors in the beak and nares of diving ducks (Butler, 1988; Jones et al., 1988; Woakes, 1988). Pre-medication with a benzodiazepine may avert it. When the response occurs



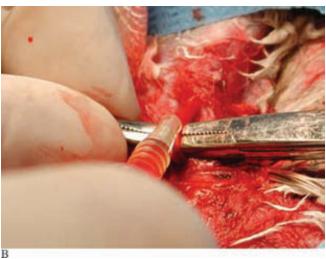


Figure 22.7. Arterial catheterization of the brachial artery in a bird. The brachial **(A)** and carotid arteries are the most common sites for arterial catheterization in birds. **B.** Percutaneous placement is utilized most commonly, but sometimes a surgical cut-down procedure is required to confirm the location of the artery.

discontinue inhalation anesthesia, remove the mask and provide 100% oxygen until bradycardia resolves.

Commercially available induction chambers can be used for birds as small as hummingbirds. Advantages of these chambers are reduced waste gas and shorter induction times. In stressed birds the chamber is covered with a towel. Alternatively, an animal carrier or the front of a hospital cage is sealed with a plastic bag and inhalant anesthetic administered for induction of large or stressed patients. Disadvantages of chambers include inability to auscult the patient, gas pollution when the chamber is opened, and trauma owing to flapping during the excitement phase of anesthesia. The latter is reduced by

padding the induction chamber and minimizing chamber size to reduce movement. Gas flow is adjusted to chamber size to provide an optimum rate of rise of the anesthetic concentration. This might be as low as 0.5 L/minute for a 1 L up to 15 L/minute for a 60-L chamber. The efficiency of the respiratory system makes high inhalant induction concentrations unnecessary. For example, the isoflurane vaporizer setting rarely needs to exceed 3%. A chamber just slightly larger than the bird is used and the patient is promptly removed after the righting reflex is lost. To facilitate monitoring, the final phase of induction is accomplished with a mask.

Pre-oxygenation

Pre-oxygenation is performed if possible and when hypoxemia may occur (i.e., upper respiratory obstruction, cardiac, pulmonary, or air sac disease). It replaces nitrogen in the respiratory system and can produce in the air sacs an oxygen reservoir 4 to 5 times normal. The benefits are achieved with greater than or equal to 1 minute of high inspired oxygen concentration in the healthy bird, but may take greater than or equal to 5 minutes in a bird with compromised respiratory function. Pre-oxygenation is accomplished with an oxygen cage or an induction chamber in the unrestrained bird, or a face mask in the physically restrained bird. Levels rise slower in an unprimed oxygen cage or induction chamber than a tight-fitting face mask with minimal dead space. If the bird is allowed to breathe room air the parabronchial oxygen levels can fall precipitously.

PRE-ANESTHETICS (TABLE 22.3)

Parasympatholytics

Several authors question the necessity of routine medication with parasympatholytics. Atropine and glycopyrrolate reduce mucus production and plug formation, but increase viscosity (Ludders and Matthews, 1996). Additionally, some practitioners avoid using anticholinergics because they increase heart rate, cardiac work, and myocardial oxygen demand. These potentially adverse cardiac effects of anticholinergics are weighed against their benefits.

Sedatives and Tranquilizers

Sedatives and tranquilizers are used to decrease anxiety and fear during induction. However, most tranquilizers lack analgesia. Additionally, most require injection and the handling and restraint may be as much as required for anesthetic induction. The merit of pre-medication is weighed against this additional stress.

Benzodiazepines Diazepam IV may cause excitement, tachycardia, and tachypnea and uptake from IM or SC injection is erratic. Midazolam is water-soluble at low pH but becomes highly lipid soluble at pH >4 so it can be given IM or SC. Midazolam (0.2–2.0 mg/kg IM) has been

Table 22.3. Injectable pre-medication/emergency, sedative, tranquilizer, and anesthetic drugs used in cage birds.

Drug	Dosage (mg/kg)	Route	Indication(s)	Comments	References
Diazepam	0.2-2.0 0.25-0.5 (appetite stimulant)	IM, IV	Most species; premedication, sedation, anti-convulsant, appetite stimulant	IM: may cause muscle irritation, absorption may be delayed. Has been used as an appetite stimulant and to improve acceptance to novel captive diets for raptors and wild passerines. Reversed with flumazenil.	Abou-Madi, 2001; Clyde et al., 1994; Massey, 2003; Rupiper and Ehrenberg, 1994; Samour, 2000; Suarez, 1993.
	2.5–4.0 7.3–8.0	PO IN	Most species/sedation Canaries	Dose divided into each nare and given slowly. Dorsal recumbency for approx. 35 mins.	Ritchie et al., 1994 Vesal and Zare, 2006
Midazolam	0.2-2.0	IM, IV	Most species/ premedication, sedation, appetite stimulant	In larger macaws the author's have noted regurgitation after doses of > 0.3–0.5 mg/kg IM. Water soluble; does not cause muscle irritation with IM use. Reversal with flumazenil IM onset 5–15 min. Higher dosages may	Abou-Madi, 2001; Day and Roge, 1996
	2.0-6.0	IM	Quail, sedation	cause profound sedation. High dosages give greatest sedation without cardiopulmonary effects, but adequate sedation also found with lower dosages, just shorter duration of sedation.	Day and Roge, 1996
	7.3-8.0	IN	Canaries, ring-necked parakeets	Dose divided into each nare and given slowly. Dorsal recumbency for approx. 17 mins. Flumazenil reduced time to recovery.	Vesal and Zare, 2006
Flumazenil	0.02-0.10	IM, IV	Most species	Benzodiazepine reversal agent.	Abou-Madi, 2001; Day and Roge, 1996; Machin and Caulkett, 1998
	0.13-0.15	IN	Canaries, ring-necked parakeets	Dose divided evenly between nares and given slowly.	Vesal and Zare, 2006
Xylazine	1.0-10.0	IM, IV	Most species, tranquilization; in combination with ketamine for anesthesia	Not recommended by itself for tranquilization and seldom used in pet birds due to adverse effects: excitement, convulsions, bradycardia, arrhythmias, bradypnea, hypoxemia, hypercarbia, death when used alone; most useful in ratites Adequate sedation often with <4 mg/kg, in smaller psittacines dosages up to 10 mg/kg may be required.	Carpenter, 2000; Clyde and Paul-Murphy, 1994; Heard, 1997; Huckabee, 2000; Ludders et al., 1989b; Samour et al., 1984; Samour, 2000
Yohimbine	0.1-0.2	IV	Psittacines, raptors	Reversal for xylazine.	Heard, 1997; Samour, 2000
	1.0	IV	Most species including psittacines, guinea fowl		Teare, 1987
	0.1-0.2 0.11-0.275	IM, IV IM	Raptors Budgerigars		Huckabee, 2000 Heaton and Brauth, 1992
	0.1-1.0	IM	Most species		Abou-Madi, 2001

Table 22.3. (Continued)

Drug	Dosage (mg/kg)	Route	Indication(s)	Comments	References
Medetomidine	0.1-0.35	IM		0.08–2 mg/kg IM associated with inadequate sedation in pigeon, yellow crowned amazon parrot. Profound respiratory depression may occur. Much higher dosages appear to be required in some avian spp when compared with mammals.	Clyde and Paul-Murphy, 1994; Pollock et al., 2001; Sandmeier, 2000
	0.25-0.35	PO	Chickens/sedation	•	James et al., 1999.
Atipamezole	0.25-0.5	IM	Most species	Reversal medetomidine.	Machin and Caulkett, 1998; Pollock et al., 2001; Samour, 2000
	1.3-1.6	IV	Chickens		James et al., 1999
Ketamine	20–50	SC, IM, IV	Psittacines, pigeons, ratites, poultry, waterfowl; restraint 30–60 min	Usually combined with an alpha ₂ adrenergic or with a benzodiazepine to improve relaxation, depth of anesthesia. Not recommended as a sole anesthetic agent due to reports of poor muscle relaxation, myoclonic contractions, opisthotonus. and violent recoveries. smaller sp. require a higher dose; large birds tend to recover more slowly.	Beynon and Forbes, 1996; Heard, 1988; Lawton, 1996; Samour, 2000
	50-100	PO	In bait for raptors	,	Samour, 2000
Ketamine/ diazepam	5-30/0.5-2.0	IM/IM, IV	Most species	Ketamine given 5–15 min after diazepam for adequate muscle relaxation.	
W /	20/1.0	IV	Toucans	For short procedures (15–20 min), give slowly.	Cubas, 2001
Ketamine/ midazolam	10-40/ 0.2-2.0	SC, IM	Most species,		
midazoiam	0.2-2.0	50, 1111	including psittacines		Mandelker, 1988

These are suggested dosages based on published information and the author's clinical experience. Species and individual variation in response to a given drug can be uncertain, so the dosage should be adjusted depending on the clinical response of the animal.

used alone for minor, non-painful procedures (i.e., radiographs) (Valverde et al., 1990). Low dosages are most often used for pre-anesthetic sedation. In pigeons midazolam (14–16 mg/kg IM) induced profound sedation and reduced isoflurane MAC approximately onethird (Smith and Muir, 1992; Smith et al., 1993). In quail midazolam (2-6 mg/kg IM) produced chemical restraint and 40 to 60 minutes of sedation at the higher dosages (Day and Roge, 1996). In ring-necked parakeets (Psittacus krameri) midazolam administered intranasally alone or in combination with ketamine produced sedation that allowed dorsal recumbency and adequate sedation for minor procedures (Vesal and Eskandari, 2006). Sedation duration is significantly reduced after flumazenil administration. The authors recommend titrating the flumazenil dose to avoid the reversal of the beneficial anxiolysis, sedation, and muscle relaxation.

Midazolam IM did not produce major alterations in cardiopulmonary function in Canada geese (Valverde

et al., 1990), quail (Day and Roge, 1996), and racing pigeons (Smith and Muir, 1992; Smith et al., 1993). Midazolam/ketamine IV produced anesthesia with full recovery in 23 minutes (Machin and Caulkett, 1998). One author (MGH) has observed midazolam (0.25–1.0 mg/kg IM) associated regurgitation in larger macaws and cockatoos. Some animals did not stop until after flumazenil administration. Benzodiazepines are either avoided in these species or a lower midazolam dosage used.

 α_2 -Adrenergic Agonists Xylazine and medetomidine are most commonly used. Their major advantage is they can be reversed with atipamezole, yohimbine, or tolazoline. α_2 -Adrenergic agonists can have profound cardiopulmonary effects, including respiratory depression, second-degree heart block, bradyarrhythmias, and increased sensitivity to catecholamine-induced cardiac arrhythmias (Altman, 1980; Ludders and Matthews, 1996; Machin and Caulkett, 1998b; Ludders, 2001).

When used alone at high dosages, xylazine is associated with respiratory depression, excitement, and seizure activity (Ludders and Matthews, 1996; Machin and Caulkett, 1998a; Ludders, 2001; Varner et al., 2004) and therefore is not recommended for sedation. In Pekin ducks xylazine produced significant respiratory depression, resulting in hypoxemia and hypercapnia and behavioral changes (i.e., moving, paddling, and picking at their enclosures) that lasted less than or equal to 45 minutes (Ludders et al., 1989b). In mallard ducks xylazine/ketamine/midazolam IV resulted in cyanotic membranes and apnea in three birds; two died and the surviving animal was reversed with atipamezole (Machin and Caulkett, 1998a).

Much higher dosages of medetomidine appear to be required compared with mammals. In pigeons and yellow-crowned Amazon parrots medetomidine (2 mg/kg IM) alone did not induce reliable sedation (Sandmeier, 2000). Similarly, in pigeons medetomidine (0.2 mg/kg) alone produced only moderate sedation but significant brady-cardia and bradypnea (Pollock et al., 2001). Also in pigeons, a medetomidine (0.2 mg/kg)/butorphanol/ketamine combination was effective in producing profound sedation. However, significant bradycardia, bradypnea, and hypothermia were observed (Atalan et al., 2002). Arrhythmias in 3/8 pigeons resolved after atipamezole reversal.

In mallard ducks medetomidine/midazolam/ketamine provided anesthesia and analgesia for 30 minutes duration when given IV, but not IM (Machin and Caulkett, 1998a). Also in ducks, medetomidine/midazolam/ketamine IV produced respiratory depression, apnea, and acidemia; one of twelve died and three required assisted ventilation (Machin and Caulkett, 1998b). Very high medetomidine dosages (less than or equal to 10 mg/kg) in mallard ducks did not increase sedation over 0.2 mg/kg (Machin and Caulkett, 1998a). One clinician reported seizures in Canvasback ducks with medetomidine IV (Caulkett, personal communication).

Because medetomidine appears to require combination with other injectable drugs for reliable effect, the advantage of rapid and smooth reversal with

atipamezole are negated. Although the mammalian dosage of atipamezole (5 times the medetomidine dose) has been shown to exhibit excellent reversal in some birds (Machin and Caulkett, 1998b), a lower ratio (2.5 times) also produces effective reversal (Machin and Caulkett, 1998a; Sandmeier, 2000). Based on the many adverse effects and disadvantages reported for this class of drugs in birds, it is recommended they be used with great caution.

Injectable Anesthetics (Table 22.3)

There are several situations in which injectable anesthetics are preferable to inhalants. Surgeries involving the beak, mouth, glottis, or trachea are complicated by the presence of an endotracheal tube. Surgery within the coelomic cavity, respiratory system, or pneumatic bones exposes personnel to high levels of inhalant anesthetics. It is also more difficult to maintain a consistent plane of anesthesia. Injectable anesthetics are also commonly used in the field owing to the ease of transport compared with inhalant anesthetic delivery equipment (see Chapter 24).

The effects of many injectable drugs are highly variable among species and individuals (Samour et al., 1984; Machin and Caulkett, 1998a). These include poor induction, inadequate muscle relaxation, cardiopulmonary depression, and prolonged or violent recoveries (Samour et al., 1984; Ludders and Matthews, 1996). The delivery route also affects efficacy and dosage. For example, in mallard ducks IM administration is not effective, suggesting poor drug uptake from the pectoral musculature. Also, no effect was identified when evaluating many drugs given intranasally in this species (Machin and Caulkett, 1998a). Elimination of injectable anesthetics depends on drug distribution, and hepatic and/or renal biotransformation and excretion (Paul-Murphy and Fialkowski, 2001).

If injectable anesthetics are used, it is vital to have accurate patient body weights to ensure accurate dosing. Also, emergency and supportive drug dosages are calculated and prepared before induction. Finally, cardiopulmonary variables are monitored closely

Table 22.4.	Analgesic drug dosages commonly used in birds.
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	Dosage	Route	Frequency	Comments
NSAIDs				
Ketoprofen	1-5 mg/kg	IM	q 8-12 hr	
Carprofen	1-4 mg/kg	SC, PO	q 12 hr	
Meloxicam	0.1-0.5 mg/kg	SC, PO	q 24 hr	Half-life in chickens and pigeons was three times as long as for ostrich, ducks and turkeys
Opioids				
Buprenorphine	0.01-0.05 mg/kg	IM	q 8-12 hr	0.1–0.5 mg/kg was ineffective in African grey parrots
Butorphanol	2.0-4.0 mg/kg	IM	q 2–6 hr	Little available information to date on dosing frequency

Note that these are suggested dosages based on published information (Graham et al., 2005; Baert and DeBacker, 2002 and 2003; McGeowen and Danbury, 1999) and the author's clinical experience. Species and individual variation in response to a given drug can be uncertain, so the dosage should be adjusted depending on the clinical response of the animal.

throughout and ventilatory equipment (i.e., endotracheal tubes and a supplemental oxygen supply) should be available if needed.

Dissociative Anesthetics

Ketamine alone is not recommended owing to poor muscle relaxation, myoclonic contractions, opisthotonus, and violent recoveries. It is usually combined with an α_2 -adrenergic agonist or benzodiazepine to improve relaxation and anesthetic depth (Muir, 1988). Ketamine may produce convulsions, excitation, and salivation in vultures, but these signs are rarely observed in other species (Salerno and van Tienhoven, 1976; Muir, 1988). Ketamine/ α_2 -adrenergic and ketamine/ benzodiazepine combinations are used for short procedures (i.e., physical examination, minimally painful diagnostics) or induction as part of balanced anesthesia (Borzio, 1973; Boever and Wright, 1975; Redig and Duke, 1976; Kollias and McLeish, 1978; McGrath et al., 1984; Ludders et al., 1989; Raffe et al., 1993; Machin and Caulkett, 1998a; Vesal and Eskandari, 2006).

Immobilization is induced with ketamine IM within 5 to 10 minutes and lasts for 5 to 20 minutes, with recovery in 40 to 100 minutes. These times are dependent on size, dose, body temperature, and health status (Paul-Murphy and Fialkowski, 2001). In mallard ducks midazolam/ketamine IV produced anesthesia with recovery in 23 minutes (Machin and Caulkett, 1998a). In chickens ketamine (120 mg/kg IM) produced no significant change in respiratory rate, but did induce bradycardia (Salerno and van Tienhoven, 1976). In redtailed hawks ketamine (30 mg/kg IM) produced no significant effect, compared with awake birds, in arterial blood gas or acid-base values, but did produce mild hyperventilation (Kollias and McLeish, 1978).

Propofol

In pigeons (Fitzgerald and Cooper, 1990) and chickens (Lukasik, 1997) propofol had a very narrow margin of safety associated with marked respiratory depression. However, at much lower dosages in turkeys (Schumacher et al., 1997) and mallard ducks (Machin and Caulkett, 1998a,b) it is relatively safe and effective if cardiopulmonary function is monitored and ventilatory support provided. Further research in other birds (see Chapter 24) has confirmed that it produces a rapid and smooth induction. However, respiratory depression and significant apnea are common (Langan et al., 2000; Machin and Caulkett, 2000; Hawkins et al., 2003; Langlois et al., 2003). Ventilatory support is recommended, regardless of whether bolus or constant rate infusion (CRI) techniques are used. Prolonged recovery, with or without moderate-to-severe central nervous system excitatory signs, may occur, particularly after the use of a CRI (Langan et al., 2000; Hawkins et al., 2003; Langlois et al., 2003). However, one study evaluating its use in the field showed smoother recoveries than with isoflurane anesthesia (Machin and Caulkett, 2000). The need for ventilatory support and the potential for excitatory and/or prolonged recoveries limit its use as a sole anesthetic. However, it has been proposed that balanced anesthesia may produce propofol-sparing effects that may reduce these disadvantages (Langlois et al., 2003). The authors suggest a calculated propofol dose be given in one-fourth increments each administered over 30 to 60 seconds. This will allow more accurate dosing and minimize apnea and hypotension.

Inhalant Anesthetics

Inhalant anesthetics offer rapid induction and recovery, ability to rapidly change anesthetic depth, and their use does not require an accurate body weight. Very little is metabolized, reducing the impact on hepatic and renal function, and recovery is independent of either. Disadvantages include pollution of the work environment and the expense of the anesthetic and associated equipment.

The minimum anesthetic concentration (MAC) necessary to prevent purposeful movement in response to a noxious stimulus in 50% of the patients is used as a measure of inhalant anesthetic potency. MAC for many species is very similar; birds require approximately the same concentration of inhaled anesthetic for an equivalent amount of stimulation as mammals.

Halothane

Halothane sensitizes the myocardium to catecholamineinduced arrhythmias as it does in mammals (Naganobu et al., 2001). These arrhythmias occur especially during induction and recovery when catecholamine release is high. Halothane depresses the responsiveness of the avian IPC to CO₂. Thus, halothane anesthetized birds may have a depressed ability to adjust ventilation in response to changes in PCO₂ (Pizzaro et al., 1990). Hypercapnia, ECG abnormalities, and hypothermia were more marked in galahs (Eolophus roseicapillus) anesthetized with halothane than isoflurane (Wijnberg et al., 1991). Ducks anesthetized with halothane had a higher tendency for hypoventilation than did chickens, but heart rates were maintained in the ducks. This suggests some mechanism other than the dive response may be involved in this hypoventilation (Ludders, 1992).

Isoflurane

Isoflurane is the inhalant anesthetic of choice. It causes less cardiovascular depression than halothane (Ludders et al., 1990; Ludders, 1992; Jaensch et al., 1999; Miller, 2005). MAC is 1.32% in chickens, 1.30% in Peking ducks, and 1.34% in sandhill cranes (Ludders et al., 1989, 1990; Miller, 2005). Despite its safety, isoflurane produces dose-dependent cardiopulmonary depression.

The concentration required to produce apnea in ducks was 1.65 times MAC and in cranes 2 times MAC (Ludders et al., 1989a, 1990). These values are less than those in dogs, cats, and horses (Miller, 2005). If surgical anesthesia is achieved in 95% of patients at 1.3 times MAC, isoflurane anesthesia has a low safety margin.

Cardiac stability is a perceived advantage. It produces peripheral vasodilation and negative inotropic effects in mammals, possibly explaining the dosedependent hypotension also observed in birds (Ludders et al., 1989a; Goelz et al., 1990; Greenlees et al., 1990; Ludders et al., 1990). Cardiac arrhythmias occurred in 75% of bald eagles (Haliaeetus leucocephalus) anesthetized with isoflurane, most during induction and recovery (Aguilar et al., 1995). Catecholamine release was suspected to be the cause. Although arrhythmias are also common in other species (Goelz et al., 1990; Aguilar et al., 1995; Korbel et al., 1998), in the authors' experience they are most common in raptors. When an electrical fibrillation model was used to investigate myocardial irritant effects of isoflurane and halothane, the former had a lower threshold for electrical fibrillation than halothane (Greenlees et al., 1990). This is surprising given that clinical experience over the years has shown this to be untrue. These findings emphasize the importance of vigilant monitoring during anesthesia.

Sevoflurane

Sevoflurane is potentially more useful owing to an even lower solubility than halothane or isoflurane. Low solubility allows faster induction and recovery, as well as more rapid changes in anesthetic depth (Thurmon et al., 1996; Miller, 2005). In pigeons, induction and recovery times were more rapid than with isoflurane (Korbel, 1998). However, in several psittacine species recovery times (time to extubation, sternal, and standing) were not significantly different between the two agents, but birds subjectively appeared less ataxic earlier (Quandt and Greenacre, 1999). The time to intubation was longer with sevoflurane (greater than or equal to 4.4 minutes) than isoflurane. However, this was attributed to administration of sevoflurane below the suspected MAC in birds. In Hispaniolan parrots the time to intubation (38 \pm 2 seconds) was rapid with sevoflurane which was attributed to the higher concentration used during induction. The time to extubation was also rapid (2.3 \pm 0.4 minutes) (Klaphake et al., 2006).

In chickens sevoflurane MAC (2.21% \pm 0.32%) was within mammalian ranges (Naganobu et al., 2000). At MAC heart rate did not change significantly and cardiac arrhythmias were not observed at less than or equal to 2 times MAC (Naganobu et al., 2000). In another study in chickens, hypotension was observed during both spontaneous and controlled ventilation. However, this effect was only dose dependent during controlled ventilation (Naganobu et al., 2003). Tachycardia occurred during spontaneous ventilation while heart rate remained

unchanged during controlled ventilation. However, in Hispaniolan parrots bradycardia was observed after 25 minutes of controlled ventilation (Klaphake et al., 2006). Hypercapnia (less than or equal to 86 mmHg) occurred with increased sevoflurane concentration during spontaneous ventilation. Hypercapnia induced increases in sympathetic tone was suggested for the maintenance of arterial blood pressures and heart rate in spontaneously ventilated birds (Naganobu et al., 2003). In both chickens and Hispaniolan parrots, a significant bradypnea was also observed (Naganobu et al., 2003; Klaphake, 2006).

Sevoflurane is less pungent than other inhalants. In human pediatric patients, it is routinely used for mask induction to prevent struggling owing to smell. Although agent cost is much higher than isoflurane, many practitioners use sevoflurane for induction, and then switch to the more cost-effective isoflurane for maintenance.

LOCAL ANESTHESIA

There are few studies evaluating local anesthetics. In chickens, successful brachial plexus nerve blockade with lidocaine 2% or levobupivacaine lasted 30 to 60 minutes in the majority of birds evaluated (D'Otaviano et al., 2006). Although local anesthetics can provide sufficient analgesia for certain procedures in some patients, the stress of handling and restraint may preclude their sole use.

Birds may be more sensitive to the effects of local anesthetics than mammals. Toxicity has been observed in birds at lower dosages (2.7 to 3.3 mg/kg) than in dogs (Hocking et al., 1997). Toxic effects were similar to those in mammals; seizures and cardiac arrest have been seen with high dosages (Ludders, 1994). Other adverse effects include depression, drowsiness, muscle tremors, vomiting, hypotension and arrhythmias, as well as central nervous system signs (e.g., ataxia and nystagmus).

Accurate lidocaine dosing is difficult in the small patient, but toxicity can be prevented by using appropriate concentrations and volumes. This usually requires diluting the commercial lidocaine solution (2%; 20 mg/ml) 1:10, and limiting total dosage to less than or equal to 2.5 mg/kg (Ludders, 1994; Hocking et al., 1997). However, it is unknown whether this dilution allows appropriate tissue drug levels and duration of analgesia (Farley et al., 1994).

Bupivacaine is used conservatively because of concerns its toxic effects take longer to resolve. In mammals the maximum recommended dosage is 2 mg/kg. In mallard ducks (*Anas platyrhynchos*) bupivacaine (2 mg/kg SC) was shorter acting than in mammals (Machin, 2001), and showed a faster absorption versus elimination rate. In addition, sequestration and redistribution suggested by increases in plasma concentrations at 6 and 12 hours, may allow for delayed toxicity. A 1:1 mixture of bupivacaine and dimethyl sulfoxide (DMSO) applied to amputated chicken beaks immediately after

amputation improved feed intake (Glatz et al., 1992). In 1.5-kg chickens intra-articular bupivacaine (3 mg in 0.3 ml saline) was effective for treating arthritic pain (Hocking et al., 1997).

Eutectic mixture of local anesthetic (EMLA) is a mixture of 2.5% lidocaine and 2.5% prilocaine for topical use. The depth of penetration of EMLA cream depends on skin contact time. In humans, toxicity is associated with improper administration (i.e., application to large surface areas and damaged skin or mucous membranes, prolonged contact time). In humans common side effects include skin blanching and local erythema. Less common are methemoglobinemia or neurological signs. In humans optimal use requires application and occlusion for 1 hour. However, shorter times appear to be effective. There have been no studies evaluating shorter contact times in animals with thin skin (i.e., birds). As with other local anesthetic preparations, the maximum dosage is calculated prior to administration. Systemic uptake may be increased by feather plucking causing skin damage and exposing feather follicles.

Monitoring

Monitoring requires frequent patient assessment and is the most important aspect of anesthesia.

Cardiovascular Heart rate is variable between individuals and species. Knowledge of expected species values is important, but trends during anesthesia are more significant. Sudden bradycardia is an indication to decrease anesthetic depth and provide supportive care (e.g., bolus fluids).

Heart rate and rhythm are monitored by an external or an esophageal stethoscope, ECG, or peripheral pulse rate. Peripheral pulse rates are determined at the brachial, medial metatarsal, or the carotid artery by direct palpation or with a Doppler ultrasonic probe (Figure 22.8). The Doppler probe is placed against the palatine artery on the dorsal palate of some species (Figure 22.8).









Figure 22.8. Peripheral pulse rates can be determined at: **A.** the brachial artery; **B.** the medial metatarsal artery; or **C.** the carotid artery either by direct pressure assessment or with a Doppler ultrasonic probe. **D.** Heart rate can also be detected by placement of the Doppler ultrasonic probe over the palatine artery on the dorsal palate of some species of raptors and waterfowl.



Figure 22.9. Indirect blood pressure monitoring can be performed using a Doppler ultrasonic probe to detect the arterial flow, a pressure cuff to occlude arterial blood flow and a sphygmomanometer to measure pressures.

ECG limb leads are placed close to the body. The alligator clips are attached to needles or stainless steel suture passed through the skin, rather than directly attaching to the skin. Heart rate and presence of an ECG trace are insensitive indicators of anesthetic depth.

Blood pressure is subjectively assessed by palpating the pulse at the median ulnar or medial metatarsal artery. Changes in pulse pressure and velocity are also reflected in volume changes when using a Doppler ultrasonic probe. Direct arterial monitoring can also be performed using these arteries. The technique is described in the vascular access section.

Indirect blood pressure monitoring is performed using a Doppler ultrasonic probe to detect arterial flow, a pressure cuff for occlusion and a sphygmomanometer to measure pressure (Figure 22.9). Alternatively an oscillometric method is used. The cuff may be placed around the thigh to occlude the tibial artery or the distal humerus for the ulnar artery. Oscillometric devices are unreliable in small patients.

Respiratory Respiratory rate and character are monitored throughout anesthesia. Ventilation is assessed by observing the frequency and range of sternal motion and reservoir bag movement. Substituting a balloon for the reservoir bag facilitates visualization of movement in patients with small tidal volumes. However, assessment of adequacy of ventilation by these methods is inaccurate. Tachypnea can be associated with small tidal volumes resulting in more dead space than pulmonary ventilation (Ludders et al., 1989).

Apnea greater than or equal to 10 to 20 seconds is an indication to decrease anesthetic depth and provide assisted ventilation. The time between respiratory and

cardiac arrest may be less than or equal to 1 to 2 minutes. Respiratory monitors that detect gas flow increase mechanical dead space.

Normal ventilation is associated with little to no respiratory tract noise. Whistling, wheezing, or harsh sounds may indicate obstruction. Many birds (e.g., ducks) will normally have an expiratory syringeal noise during IPPV.

End-tidal carbon dioxide (PETCO₂) monitoring is used to determine ventilatory efficacy. Ideally the sampling port is located inside the endotracheal tube, but it should not increase airway resistance. Side-stream capnographs draw samples at a rate of 50 to 200 ml/minute. This rate is usually fixed, but some allow alteration. In small birds even this low flow may exceed minute ventilation.

There is good correlation between PETCO₂ and PaCO₂, with PETCO₂ slightly exceeding PaCO₂ (Edling et al., 2001; Pettifer et al., 2002; Hawkins et al., 2003). This can occur in the avian parabronchus, but is impossible in alveolar gas exchange (Powell and Whittow, 2000). Carbon dioxide diffusion occurs across the length of the parabronchus, with a higher diffusion rate at the inspiratory and a lower rate at the expiratory end. Since arterialized blood returning to the heart is a mix of capillary blood draining the entire length of the parabronchus, $PaCO_2$ can be less than $PETCO_2$ in ideal cross current exchange. The capnogram provides important information regarding trends in $PETCO_2$.

Pulse oximetry has not been validated. The absorption characteristics of oxygenated and deoxygenated avian and human hemoglobin are different, resulting in underestimation of hemoglobin saturation (Schmitt et al., 1998). In pigeons, hemoglobin saturation trends were consistent, but values did not correlate with those derived from blood gas analyses and calculation (Schmitt et al., 1998).

Anesthetic Depth The cere, beak, head, cloaca, and digits are used to assess response to pain. Surgical incisions and needle pricks evoke less response under anesthesia than for mammals. Withdrawal reflexes include toe pinch, stimulation of the interdigital tissue, pinching the scaly areas of the skin, cloacal pinch, and feather plucking. Slight corneal and palpebral reflexes are maintained at a surgical plane; their absence may indicate excessively deep anesthesia. In raptors anesthetized with propofol contour feather plucking did not initiate a response in any bird at any time period during CRI (Hawkins et al., 2003). Rather, toe clamping was a better guide to anesthetic depth.

Glucose Blood glucose is monitored when possible, particularly during prolonged procedures. In auklets, the values determined by four handheld human glucose monitors were comparable to Chemstrip BG. However, values for all systems were 33% less than those determined by a reference chemistry laboratory (Lieske et al., 2002). Blood storage in heparin was preferable to ethyl-

endiamine tetra-acetic acid (EDTA). Stored blood glucose values were stable for 4 hours.

Recovery

Recovery complications are usually associated with long anesthetic procedures (greater than or equal to 0.5 to 1.0 hours), emphasizing the importance of minimizing anesthetic time. The vaporizer is turned off at the end of the procedure and circle breathing systems flushed with oxygen. This flushing is unnecessary with a nonrebreathing system. The patient remains connected to the breathing system and oxygen as long as possible. Signs of recovery include muscle fasciculations, then wing and leg movement. Once jaw tone returns the bird is extubated to prevent severing the endotracheal tube. Once extubated, an anesthetic face mask with or without the rubber diaphragm is placed over the bird's head to continue oxygen supplementation. Most are placed loosely in a towel and held upright to minimize selftrauma and regurgitation. Respiration is monitored during towel restraint to ensure adequate sternal movement. Once recovered, the bird is placed in a warm, well-oxygenated environment for continued recovery. A quiet dark environment minimizes stress and movement.

ANALGESIA

See Chapter 3.

Pain Recognition

Pain recognition is critical for providing timely analgesic selection. It requires consideration of age, sex, and species differences, as well as individual behavior and environmental factors. Birds either hide painful or exhibit different behaviors outside their home cage. Pain assessment must also account for different types and sources of pain (i.e., acute, chronic, visceral, and somatic).

The observer must be familiar with normal and abnormal behavior to assess pain. Social species exhibit pain behaviors dependent on the group social dynamics (Clyde and Paul-Murphy, 1994). Predatory species exhibit abnormal behaviors more readily than prey species. Painful behaviors attract unwanted attention from predators, requiring masking to survive. The clinician is viewed as a potential predator.

Many clinical signs are associated with pain, including change in temperament (either aggressive or passive), restlessness, reduced mobility or reluctance to stand or perch, lethargy, hunched appearance, sleep deprivation, tachypnea, and lameness. Reduced food consumption may occur, and body weight should be monitored. Animals with abdominal pain can exhibit tensing with a "tucked up" or "hunched" appearance. Birds may either avoid a painful body area or bite/chew it. Decreased or over-grooming (feather-picking) may occur

at a painful site. Vocalization and writhing occur rarely during acute or severe pain. Owners often describe reduced vocalization in birds with traumatic injuries.

Few physiological variables are consistent indicators of pain. In chickens during feather plucking, heart rates and respiratory rates were variable, but increased blood pressure was a reliable indicator (Gentle and Tilston, 1999). Catecholamines are well-recognized humoral indicators of stress, but vary among individuals and species because of differences in adrenal content (Harvey et al., 1984). Corticosterone significantly increases in birds following pain. They also elevate with handling (Heatley et al., 2000).

A set of universal questions are used to determine if a patient is in pain:

- 1. Would the lesion or procedure be painful to any species?
- 2. Is the lesion or procedure damaging to tissues in any species?
- 3. Does the patient display any abnormal behavioral responses?

If the answer to any of these questions is yes, then the veterinarian must assume their patient is in pain and an analgesic plan should be developed.

Opioids Most opioid analgesics are used parenterally because of their overall poor oral bioavailability associated with the first pass effect. Analgesia is species and intra-species variable at equipotent dosages. In pigeons, regional distribution of μ , κ , and δ receptors in the forebrain and midbrain were similar to mammals (Reiner et al., 1989). However, the κ and δ receptors were more prominent in the pigeon forebrain and midbrain than μ and 76% were κ (Mansour et al., 1988). This may explain, in part, why birds appear not to respond to μ agonists. However, in day-old chicks receptor distribution was markedly different, suggesting either age or species effect (Csillag et al., 1990). Birds may not possess distinct μ and κ-receptors or the receptors may have similar functions. This would explain why chickens are unable to discriminate μ and κ agonists and the isoflurane-sparing effects of μ and κ agonists appear similar to mammals (Concannon et al., 1995).

Morphine at high dosages (200 mg/kg) produced analgesia in chicks (Schneider, 1961). In another study, it produced a similar, but variable level of analgesia at dosages approximating those recommended in other species (Hughes, 1990a,b). Variable morphine responses have been detected between chicken breeds (Fan et al., 1981). Analgesic effects were observed in one breed, but two others exhibited hyperalgesia at the same dosage (Hughes, 1990a). In a domestic fowl arthritis model, intraarticular injection of morphine (1–3 mg) showed no significant antinociception. However, it is unclear whether synovial fluid pH differences may have affected drug activity (Gentle et al., 1999).

In Hispaniolan parrots anesthetized with sevoflurane, pre-operative butorphanol administration did not show significant anesthetic (including time to intubation and extubation) or cardiopulmonary effects. Butorphanol (1 mg/kg) produced an isoflurane-sparing effect in cockatoos and African grey parrots, but less in blue-fronted Amazons (Curro, 1994; Curro et al., 1994; Paul-Murphy et al., 1999). In African grey parrots butorphanol (1-2 mg/kg) increased withdrawal threshold response to electrical stimuli (Paul-Murphy et al., 1999). Pharmacokinetic and pharmacodynamic data suggest 2–4 hour dosing intervals are appropriate in mammals. In red-tailed hawks and great-horned owls butorphanol (0.5 mg/kg IV) had a half-life of 0.93 (0.94 IM) and 1.78 hours (1.84 IM), respectively (Riggs & Hawkins, unpublished data). In Hispaniolan parrots administered butorphanol (5 mg/kg SC) serum concentrations were undetectable at 2 and 12 hours (Sladky et al., 2006). These studies indicate very frequent (impractical) butorphanol dosing is required to maintain drug levels in birds. In Hispaniolan parrots a long acting liposomeencapsulated, butorphanol tartrate formulation was safe and effective for up to 5 days following SC administration (Sladky et al., 2006). Unfortunately, this formulation is not commercially available.

Early anecdotal reports suggesting buprenorphine (0.01 to 0.05 mg/kg IM) was an effective analgesic in birds (Jenkins, 1993; Schaeffer, 1994) are contradicted by more recent studies. In a domestic fowl arthritis model, intra articular administration of buprenorphine (0.05 to 1.0 mg) produced no significant antinociception (Gentle et al., 1999). In African grey parrots a high dosage (0.1 mg/kg IM) achieved plasma concentrations in the human analgesic range for 2 hours (Paul-Murphy et al., 2004), but it did not affect withdrawal response to an electrical stimulus (Paul-Murphy et al., 1999).

Non-steroidal Anti-inflammatory Drugs Ketoprofen is most commonly used parenterally because of limited oral pharmacokinetic data and difficulty in accurately dosing in small species. In Japanese Quail (*Coturnix japonica*) ketoprofen (2 mg/kg PO, IM, IV) showed very low oral (24%) and IM (54%) bioavailability and the shortest half-life for any species (Graham et al., 2005). Additional studies are needed to determine whether drug formulation or interspecies physiological differences account for these differences. In mallard ducks ketoprofen (5 mg/kg IM) decreased blood thromboxane B2 levels for approximately 12 hours (Machin et al., 2001).

Research is needed to determine appropriate dosage, and dosing route and frequency for carprofen. Carprofen SC improved the locomotion of lame domestic fowl in a dose-dependent manner (McGeowen et al., 1999) and lame birds self-selected food containing Carprofen (Danbury et al., 2000). The author has used

this NSAID (1–4 mg/kg PO, SC and IM q 12–24 hours) short-term (less than 7 days) in many species.

In ring-necked parakeets oral meloxicam bioavailability approached 100% (Wilson et al., 2004). A significant variation in meloxicam half-life has been reported. In ostriches meloxicam IV had a very short half-life (0.5 hours) compared with ducks, turkeys, pigeons, and chickens (Baert and De Backer, 2002, 2003).

Celecoxib (10 mg/kg PO q 24 hours) has been used in birds with clinical proventricular dilatation disease (PDD) (Dahlhausen et al., 2002). Treatment durations of 6 to 12 weeks are recommended. Clinical improvement is observed within the first 7 to 14 days with gradual resolution of clinical signs over the course of therapy. Premature treatment cessation may result in recrudescence of clinical signs. However, in some birds clinical improvement resumed with additional medical therapy.

Balanced or Multi-modal Analgesia

Combinations of drugs acting at different points in the nociceptive system are more effective and less toxic than either drug alone. For example, opioids act centrally to limit nociceptive input, whereas NSAIDS act peripherally to decrease inflammation, limiting nociceptive information that enters the CNS. Synergy has been demonstrated in laboratory animals (Malmberg and Yaksh, 1993) and is being tested clinically.

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23

Free-Living Waterfowl and Shorebirds

Daniel M. Mulcahy

INTRODUCTION

Waterfowl (ducks, geese, and swans) are aquatic birds within the Family *Anatidae*, Order *Anseriformes*. They vary greatly in body mass, from several 100 g to more than 13 kg (Olsen, 1994). Shorebirds belong to the Order *Charadriiformes*, of which three species of the Family *Scolopacidae* are discussed here.

The introduction of isoflurane to avian medicine in the 1980s made general anesthesia safe enough to permit long surgical procedures. Several papers pertinent to waterfowl and shorebird anesthesia and analgesia have been published recently (Heard, 1993; Heard, 1997; Machin and Caulkett, 1998a; Clyde and Paul-Murphy, 1999; Abou-Madi, 2001; Paul-Murphy and Ludders, 2001; Machin, 2004; Gunkel and Lafortune, 2005; Machin, 2005a, 2005b).

Birds feel pain in much the same physiochemical ways as do mammals, which means the principles of anticipating and treating pain in mammals are always applied (see Chapter 4). Sufficient progress in avian anesthesia has been made so there is no excuse for not using appropriate regimens for surgery in birds (Mueller, 1982). Compared with poultry, pigeons (*Columba livia*), quail (*Coturnix* sp.) and psittacines, waterfowl pain has received little attention (Machin et al., 2001). Almost no information is published for shorebird anesthesia and analgesia. Species and individual variation is expected; a routine "one dose fits all" approach should be avoided.

THE PATIENT

The influence of body condition on anesthetic morbidity has received little attention. Obesity, a very common problem in domestic waterfowl, reduces tidal volume because of air sac compression. This can lead to hypercapnia, respiratory acidemia, and possible death (Phalen et al., 1996). However, free-living birds have increased intracoelomic fat at times during their life

cycle. Shorebirds (e.g., bar-tailed godwits, *Limosa lapponica*) may have a fat mass of 41% of their body weight at the beginning of their very long migrations (Gill et al., 2005).

Birds at different stages of their life cycle have different anesthetic risks. Brooding hens trapped on the nest, and birds at the end of a long migration are often dehydrated and in poor body condition. Over-wintering birds and those caught after storms may be suffering nutritional stress. Harlequin ducks (Histrionicus histrionicus) caught during the winter had more anesthetic complications and deaths than those caught in the fall (Mulcahy, unpublished data). Harlequin ducks caught after a storm lasting greater than or equal to 3 days also exhibited more anesthetic complications and deaths than those caught during good weather or after storms lasting less than or equal to 2 days (Mulcahy, unpublished data). The ducks caught after the 3-day-long storm were hypoglycemic and hypokalemic. This was probably owing to higher exertion and reduced feeding opportunities during the storm, but the deficits were made up within a few days. Ideally, avian blood glucose levels are greater than or equal to 200 mg/dl before anesthesia. Inexpensive (less than or equal to \$100), overthe-counter blood glucose monitors require little blood, give rapid results, and are relatively accurate (Lieske et al., 2002).

To reduce acute stress capture and handling are done quickly and competently; the bird is handled gently and anesthetic induction begun as soon as possible. All equipment and supplies are readied before removing the bird from the holding container. A highly stressed bird is more likely to resist anesthetic induction.

FASTING

Fasting before anesthesia and surgery has been both recommended and discouraged. A fast of 3 to 12 hours is recommended to empty the crop to reduce

regurgitation and aspiration (Harrison, 1991; Curro, 1998; Redig, 1998). In wild-caught waterfowl a preinduction fast of 1 hour is sufficient for the crop to clear (Mulcahy, unpublished data). As a precaution, the anesthetized bird is laid on a foam pad or other platform slightly elevated (3 cm) above the anesthetic table. The bird's head is positioned on the table lower than the rest of its body. This lessens aspiration of refluxing crop or gastric contents.

ANESTHETIC ENVIRONMENT

Patient stress and anesthetist distractions are minimized during the peri-anesthetic period. The awake or recovering birds are caged in an area that is quiet and protected from the elements. Wild-caught birds are housed outdoors in containers placed where human traffic is minimal and they cannot be inadvertently kicked or shoved. Lightly anesthetized birds are roused by loud noises (e.g., laughter, motor noises, and raised voices), which should be avoided.

PHYSICAL RESTRAINT

Physical restraint is used in captive and wild birds if the procedure is of short duration, causes minimal pain or distress, and the holder is experienced. Of paramount importance is bird and handler safety. The main goal is completion of the desired procedure in the minimum time required, with the least stress on the bird. However, restraint may not always be minimal or even gentle; wild birds are especially alert for a relaxed grip. They will then make an explosive attempt to escape or inflict harm upon the restrainer and person performing the procedure. A firm grip and proper technique minimize injury to all species involved. Fortunately, restraint of waterfowl, shorebirds, and seabirds is much less riskier than some other avian groups (e.g., raptors, psittacines, and large ratites).

Covering the eyes with a hood or a stocking reduces stress during transportation and handling. However, these covers are sometimes dislodged by the bird shaking its head. Ducks and geese are picked up for short periods by grasping the base of both wings in one hand and supporting the feet and body with the other (Figure 23.1). This places considerable stress on the wings and is used only with additional support and not for fractious birds that may fracture a wing. It is a useful technique for controlling birds as they are removed from a transport container.

Ducks and some geese are conveniently held by tucking their heads under a wing, which appears to cause mild sedation. For additional brief restraint "hook-and-loop" strapping is wrapped snugly around the bird incorporating both folded wings. Care is taken not to restrict respiration. Restrained birds can then be weighed on a scale (Figure 23.2).



Figure 23.1. Restraint technique used for ducks and small geese. The humeri are grasped with the fingers of one hand. For heavier birds, the other hand should be placed under the feet to support the weight of the bird. Using this technique, birds should not be held for more than 1 or 2 minutes to avoid damage. (Photograph courtesy of Scott Larsen.)

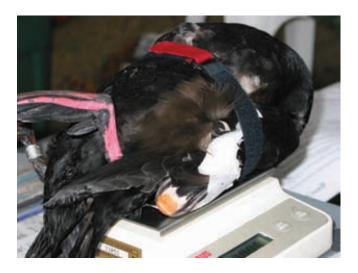


Figure 23.2. Temporary restraint of a male surf scoter (Melanitta perspicillata), here used to weigh the bird on a scale, by tucking the head under a wing and wrapping the bird snugly with "hook-and-loop" strapping. Care is taken to avoid interference with respiratory excursions of the keel and the duration of such restraint should be measured in seconds. (Photograph courtesy of Dan Esler.)

For anesthetic induction the bird is removed from the holding container and placed on a table. It is manually restrained by holding the folded wings and exerting slight downward pressure. Most birds will not struggle if the restraint does not vary. Handling during capture and processing can cause significant hyperthermia related to the environmental temperature (Phalen et al., 1996;

Davenport et al., 2004). Plumage provides superb heat retention, especially in waterfowl and other species adapted for life in the arctic. Excess heat is lost by evaporation through panting, transdermally in featherless areas, and through the feet where blood circulation is under partial voluntary control.

RESPIRATORY CONTROL

Waterfowl have been used extensively in avian respiratory studies. A physiologic feature in waterfowl, and other birds, is intrapulmonary chemoreceptors that respond to PCO₂. They interface respiratory control and gas exchange by being more responsive to alterations in PCO₂ than PO₂ (Fedde et al., 1974; Hempleman and Burger, 1984; Hempleman et al., 1986). These receptors provide feedback control to ventilation and match respiration with metabolism (Shoemaker and Hempleman, 2001). Intrapulmonary chemoreceptors are afferent vagal neurons sensitive to PCO₂ tension variation in different parts of the avian lung (Hempleman and Bebout, 1994; Hempleman et al., 2000; Hempleman et al., 2003). Receptor response is actually to H⁺, from CO₂ hydration, and the receptors are inhibited rather than excited (Powell et al., 1978; Adamson and Burger, 1986; Bebout and Hempleman, 1999). Intrapulmonary receptors are located within the parabronchial gas exchange area (Scheid et al., 1974; Nye and Burger, 1978). More than 95% of receptors are located in the caudal lung, an area that experiences marked CO₂ fluctuations during respiration (Scheid et al., 1974). Intrapulmonary chemoreceptors are part of a reflex arc that inhibits respiration when intrapulmonary PCO2 decreases (Burger and Estavillo, 1978).

MONITORING

Monitoring begins as soon as a bird is placed in front of the anesthetist, with observation of respiration and attitude. It ends when the bird is fully recovered and returned to its source. As is often stated, there is no better monitoring technique or device than a trained, experienced, and attentive anesthetist to assure the greatest patient stability and safety. Changes in anesthetic depth, body temperature, and cardiopulmonary status occur quickly in birds and must be quickly identified and responded to. In field work, a biologist is usually

drafted as an esthetist and given on the job training. To assure maximum efficacy it is preferable to concentrate acquisition of an esthesia experience in one person, rather than rotate the responsibility between multiple biologists. A trusted an esthetist allows the surgeon to concentrate on their job, contributing to quality work and reduced an esthesia time.

There are several schemes for staging anesthetic depth (Korbel, 1998; Sandmeier, 2000). In practice, most are too complicated, especially for relatively short procedures, and only serve to divert the attention of the anesthetist away from directly observing the patient. A simpler scheme for field work with a biologist anesthetist is given in Table 23.1 (Rosskopf and Woerpel, 1996; Curro, 1998). Successful induction has occurred when the legs and wings can be extended without being withdrawn and in most, this signals readiness for intubation.

Once intubated the appropriate monitoring instrumentation is applied. Respiratory monitors, stethoscopes, electrocardiographs, capnographs, blood gas analyzers, blood pressure monitors, and cloacal and esophageal temperature probes have been used to assess anesthetic status of waterfowl (Figure 23.3). Deciding the instrumentation to use depends on practicality and procedure length. It is contrary to the best interests of the patient to significantly extend anesthetic duration to place additional monitoring sensors and instruments. The anesthetist must understand that no electronic or mechanical monitor is to be trusted.

The essential physiological variables to monitor include heart rate and rhythm, respiration rate and depth, and body temperature. Reference values for cardiopulmonary variables vary between species and conditions; representative values are given in Table 23.2.

Respiration is evaluated by observation. Depth is judged by the extent of sternal movement. Movement of the re-breathing bag does not reliably reflect occurrence and depth of respiration, as the cuffless endotracheal tube may not form a sufficient seal. Arterial blood gas analysis is the definitive means of evaluating ventilation, but is rare in the field.

Tracheal secretions tend to be very thick. Clicking or gurgling noises indicate partial tracheal or endotracheal blockage; the endotracheal tube is withdrawn and cleaned if necessary. Sometimes the plug is located in the trachea instead of the tube. Complete tracheal

Table 23.1. Simplified anesthesia levels of birds.

Induction	Muscle relaxation, lowered head, drooping eyelids, wings and legs can be extended without being withdrawn.
Light	No response to positional change; corneal, palpebral, and pedal withdrawal reflexes present; no volitional movement.
Medium	Respirations slow and deep; palpebral reflex absent; corneal and pedal reflexes sluggish or absent.
Deep	Respirations very slow and progressively shallow; reflexes absent.

The stages are continuous.

From Curro TG. Anesthesia of pet birds. Semin Avian Exot Pet Med 1998;7:10-21.



Figure 23.3. A lesser Canada goose (Branta Canadensis) anesthetized with isoflurane with anesthetic circuit shown. The patient, prepared for surgery, is being electronically monitored with a digital thermometer, capnograph, and pulse oximeter, and a blood sample is being drawn from the jugular vein for blood gas determination.

obstruction (as from a plug) is suggested by marked inspiratory and expiratory efforts with little to no air movement. In many cases, the anesthetist can force air past the obstruction with positive pressure, but the material re-obstructs the tube. End-tidal CO_2 readings will be low or zero, despite assisted ventilation. If this occurs, the tube is removed immediately and either replaced or cleaned and reinserted. Tracheal mucous plugs are sometimes removed by inserting a longer, smaller diameter endotracheal tube, rotating, then withdrawing with the mucus plug attached. Obstructions occur more often with dehydration that thickens secretions. Wild birds held for hours prior to surgery are assumed to be dehydrated, as they will rarely drink water provided in a holding container.

Electronic monitors are available that connect to the endotracheal tube to monitor respiratory activity (see Chapter 6). These instruments also display a calculated respiratory rate, but this should not be uncritically accepted. Manipulations of the bird's body can cause excursions of air through the trachea that are not part of the respiratory cycle. Observation of the graphic wave form of a capnograph can confirm observed respiration rates that reflect a true respiratory cycle (Figure 23.3). However, not every capnograph is accurate at small tidal volumes (see Chapter 6). Capnography is considered accurate only during positive pressure ventilation (Sap et al., 1993). The end tidal partial pressure of CO₂ slightly underestimates the arterial partial pressure of CO₂ (Edling et al., 2001). When monitoring with a capnograph, manual or positive pressure ventilation is adjusted to keep end-tidal CO₂ partial pressures at 30 to 45 mmHg (Edling et al., 2001).

The purpose of cardiovascular monitoring includes assuring the heart is beating and the blood is circulating. Pulses are palpable at the tibiotarsal or elbow (cubital)

joints, if the hands of the anesthetist and extension of a leg or wing will not disturb the procedure. A stethoscope, esophageal stethoscope, electrocardiograph, or Doppler flow detector is used for cardiovascular monitoring. In practice, only a single electronic monitor is used

Pulse oximetry is undependable because of motion artifact, inaccuracy, lack of calibration to avian hemoglobin, and discontinuity of values during surgical emergencies (Schmitt et al., 1998). Pulse oximeters calibrated for human blood will be expected, at the same level of oxygen saturation, to give a lower saturation value for avian blood (Schmitt et al., 1998). For routine monitoring the relative inaccuracy of oxygen saturation is not critical and the pulse oximeter can be used to monitor trends in heart rate and oxygen saturation. Relying solely on pulse oximetry to monitor birds anesthetized with isoflurane in 100% oxygen is inadequate as they may be poorly ventilated despite adequate oxygenation (Edling et al., 2001).

Some commercial pulse oximeters measure very rapid heart rates, but it is advisable to query oximetry manufacturers about the possibility of modifying a unit to assure that function. Having a display of heart rate and oxygen saturation levels is valuable for monitoring avian anesthesia. It is often difficult to find a suitable site for placing the pulse oximeter probe. The interdigital webbing of the feet is used, but the presence of pigment may make the site unsuitable for a transmittance probe. Similarly, clamp probes are placed on the tip of the upper bill of ducks with lightly pigmented bills (Figure 23.4). Reflectance probes are placed into either the esophagus or cloaca. Maintaining a constant, proper position with reflectance probes is a problem; the anesthetist may have to make frequent adjustments to assure adequate tissue surface contact.

Auscultation of the heart is a simple and direct means for monitoring heart rate and rhythm. The large pectoral muscle mass of waterfowl reduces transmission of cardiac sounds; the stethoscope diaphragm is placed on the dorsal thorax, lateral thorax, or thoracic inlet. However, placing a stethoscope under the surgical drape may be disruptive to the surgeon. The easiest cardiac monitor to use is an electronically amplified, battery powered, esophageal stethoscope (Audio Patient Monitor, A.M. Bickford, Inc., Wales Center, NY). The sensor is a hollow plastic tube with multiple openings at the distal end, covered with a plastic cuff. Sensor tubes are available in a variety of diameters; the largest tube compatible with the esophagus is used for the best signal. The tube is inserted to the level of the heart (Figure 23.3). Positioning is evaluated by listening to the volume and clarity of the signal. The long necks of waterfowl and shorebirds facilitate intra-operative adjustments without disturbing the surgeon. An audible signal of the heart beat allows everyone involved in the surgery to monitor the patient. The sensor tube is placed

Machin and Caulkett, 1999 Ludders et al., 1989b Valverde et al., 1990 Mitchell et al., 2001 Ludders et al., 1990 Goelz et al., 1990 Seaman et al., 1994 Shams et al., 1990 Rode et al., 2003 Reference HCO_3 22 ± 1 15-26 24 ± 1 22 $PaCO_2$ (mmHg) 32 ± 1 27-41 40 ± 3 29 ± 2 $30\pm1\\30\pm3$ 31 ± 1 30 (mmHg) 101 ± 2 84 ± 12 100 ± 2 92 ± 2 88 ± 3 102 ± 2 98 ± 1 7.45 ± 0.02 7.42 ± 0.02 7.47 ± 0.01 7.46 ± 0.01 7.40 ± 0.04 7.36-7.50 7.44 pHa Mean BP (mmHg) 155 ± 12 128 ± 14 124 ± 13 130 ± 5 147 ± 24 Diastolic BP (mmHg) 128 ± 7 127 ± 25 Systolic BP (mmHg) 194 ± 10 170 ± 26 Body Tempera- 40.2 ± 0.6 40.9 ± 0.4 39.0 ± 0.8 ture (°C) 41.3 ± 0.2 41.6 ± 0.2 Resp. Rate 16 ± 2 21 ± 3 19 ± 1 19 ± 4 17 ± 4 (BPM) 6-13 Heart Rate 213 ± 8 218 ± 32 158 ± 48 190 ± 17 (BPM) platyrhynchos) Canada goose canadensis) Canvasback Pekin duck (Branta (Anas duck Species

Table 23.2. Mean cardiopulmonary and blood gas values with SD (\pm) or range (-) for normal waterfowl.



Figure 23.4. Placement of a pulse oximeter transmittance probe on the bill of a female mallard duck (Anas platyrhynchos). This technique works when there is little or no pigment on the bill. (Photograph courtesy of Scott Larsen.)

immediately after intubation. Sometimes respiratory sounds are also heard. Diminished or no heart sounds are usually due to inadvertent displacement of the sensor. However, the anesthetist must not spend too much time adjusting the sensor before raising the alarm about potential cardiac abnormalities.

An ultrasonic Doppler flow detector (Parks Medical, Parks Medical Electronics Inc., Aloha, OR; Minidop, Jorgensen Laboratories, Inc., Burlington, WI) is most commonly used for cardiac monitoring. The ultrasound probe is commonly taped over the cranial tibial artery, but the superficial ulnar artery, at the distal humerus, and the carotid artery are also used (Zantop and Bowles, 2000; Lichtenberger, 2005). The Doppler flow detector allows indirect monitoring of systolic blood pressures, using the appropriate pressure cuff size (40% of appendage circumference) around the leg proximal to the probe. Reference blood pressure values have been determined for a few species of waterfowl (Table 23.1). Diastolic, and therefore mean, blood pressure cannot be obtained with this method. Birds with systolic blood pressures less than or equal to 90 mmHg or greater than or equal to 145 mmHg are evaluated for causes of hypotension and hypertension, respectively (Lichtenberger, 2005). Hypovolemia is treated with bolus administration of crystalloids (10 to 20 ml/kg) or colloids (5 ml/kg) until systolic pressures are restored (Lichtenberger, 2004). For immediate effect, fluids are given IV or intraosseous (Valverde et al., 1993).

Digital thermometers are more useful than traditional thermometers because their displays are easier to read. Digital thermometers are placed in either the cloaca or deep in the esophagus (Figure 23.3). Cloacal sensors are taped in place, but the tape is easily dislodged by fecal fluid and the thermometer is difficult to read if covered by a surgical drape. Digital thermometers

with long, flexible extension sensors (e.g., Electrotherm Model 99A, Cooper Instrument Corp., Middlefield, CT) are preferred for esophageal placement. To read core temperature the sensor is inserted until it is past the thoracic inlet. Normal body temperature in waterfowl is 40°C to 42°C, but tends to decline during anesthesia.

MAINTENANCE OF BODY TEMPERATURE

Body temperature maintenance within a normal range begins with a patient that is dry, clean, and minimally stressed. Hypothermia is more likely to occur in a patient with feathers wetted during capture and handling or fouled by feces and urine during transportation. Conversely, a bird severely stressed during capture, transported in a poorly ventilated container, and held for hours before a procedure at high environmental temperatures is very likely to be hyperthermic. In the author's experience with Arctic waterfowl and shorebirds, that hyperthermia occurs more commonly than hypothermia, which is fortunate as it is more easily treated.

During normal respiration the turbinates are warm and humidify inspired air (Schmidt-Nielsen et al., 1970). The efficiency of evaporative heat exchange by the turbinates is such that the nasal surface temperature may be less than ambient air (Jackson and Schmidt-Nielsen, 1964). During exhalation, water and heat loss is minimized by the air being cooled and supersaturated as it passes over the turbinates. The reduction in evaporative water loss ranges from 55% to 71% in birds (Geist, 2000). Exhaled air temperature at the external nares averaged 19.6°C less than or equal to core, whereas oropharyngeal temperature measured only 3.5°C lower, indicating the trachea is minimally involved in heat exchange (Geist, 2000). The condensed moisture and heat recovered at the turbinates are returned to the body. In the intubated bird during anesthesia breathing is shifted from nasopharyngeal to oropharyngeal, bypassing the countercurrent heat-exchange and moisture recovery mechanisms in the nasal cavity. This accelerates heat and moisture loss. The type of breathing system used for avian anesthesia has little effect on body temperature loss. Pigeons anesthetized with three different systems had lost about 1.7°C by 45 minutes and 2.7°C at 90 minutes (Boedeker et al., 2005).

Correction of abnormal body temperatures is done as soon as it is recognized. Hyperthermia is treated by wetting the unfeathered legs and feet with isopropyl alcohol. In severe hyperthermia, rapid correction requires that other concerns be ignored. It may be helpful to also wet the axilla with alcohol, despite the risk of removing waterproofing of the feathers.

Correction of hypothermia is more difficult, and is best avoided. If body temperature decreases suddenly, dislodgment of the temperature sensor from within the thorax is suspected first. To treat a hypothermic bird, apply external heat to the exposed skin of the feet and lower legs. Bags of water or saline heated to less than or equal to 43°C, or chemical heat packs wrapped in a layer of cloth are placed on the feet. Leaks in the bags are avoided to prevent feather wetting that will exacerbate hypothermia. Waterfowl reduce heat loss by decreasing blood flow to their hind limbs, making external heat application to the feet less efficient. Hypothermic birds recover very slowly from anesthesia. They are held wrapped in a towel to conserve body heat during recovery. It is best to correct the body temperature abnormality during anesthesia rather than to expect the postanesthetic patient to recover on its own. Hypothermic birds are recovered and re-warmed with caution and with constant observation. Re-warming reverses peripheral vasoconstriction and increases metabolic demand for glucose (Heard, 2000). Deaths of hypothermic birds that occur within several hours of the end of anesthesia may be caused by such effects (Heard, 2000).

Efforts to reduce thermal loss under anesthesia usually involve placing the bird on an insulated pad, a heated circulating water mattress, or wrapping in bubble wrap (Harrison, 1994). These methods have little effect because of the high insulative value of feathers. A radiant energy source placed just above anesthetized birds was the only effective technique for maintaining a constant body temperature (Phalen et al., 1996; Rembert et al., 2001). The effectiveness of radiant heat was demonstrated in a sun conure (*Aratinga solstitialis*) that died of heat stroke (body temperature of 48.1°C) during surgery under an unusually hot surgical lamp (Hofmeister and Hernandez-Divers, 2005).

RECOVERY

For recovery, the anesthetized bird is positioned in lateral to slightly ventral recumbency. The bird remains intubated and respiration is assisted until it shows controlled, voluntary motion and objects to the presence of the endotracheal tube. The tube and esophageally placed monitoring sensors are removed at that time. Newly extubated birds remain sedated by the anesthetic and may become quiescent.

Many recovering birds go through a period of disorientation, wing-flapping, and struggling (emergence delirium) that may result in self-inflicted trauma (Curro, 1998). To avoid this, recovering birds are wrapped in a towel (unless hyperthermic) and observed closely for continued respirations. Only when the bird holds its head erect and steady is it replaced in the recovery container. It is then regularly observed for flexion of its head and neck that may obstruct the airway. If this occurs, the bird is re-positioned or removed from the recovery container and held until fully recovered. Recovery time depends on the choice of anesthetic, anesthetic duration, and extent of physiological alteration that has

occurred. A bird that is hypothermic, hypoglycemic, or that has impaired drug elimination mechanisms will take longer to recover (Heard, 2000).

ANTICHOLINERGICS

Anticholinergic drugs (atropine or glycopyrrolate IM) reduce pharyngeal and tracheal secretions, but may also increase their viscosity. Consequently, they are recommended only for treatment of bradycardia.

INHALATION ANESTHESIA

Inhalation anesthetics offer the advantages of familiarity and ready availability of equipment for veterinarians. When using an inhalation anesthesia in birds, an agent-specific vaporizer and a non-rebreathing circuit (e.g., Bain) are usually used. Anesthetic breathing systems are disinfected between uses, but are thoroughly rinsed to remove residual toxic substances that may damage the respiratory system (Greenacre, 1993).

Isoflurane has been the primary inhalant anesthetic for birds since the mid-1980s (Bednarski et al., 1985; Ludders et al., 1989a, 1988b). Others (i.e., methoxyflurane and halothane) are rarely used now because their manufacture has been discontinued (Ludders et al., 1988a; Goelz et al., 1990; Greenlees et al., 1990). The recently introduced sevoflurane is increasingly used in clinical settings. Because of its lower blood gas partition coefficient, induction and recovery of birds occur more rapidly than with isoflurane (Korbel, 1998; Quandt and Greenacre, 1999). Sevoflurane is less pungent than isoflurane for human beings (TerRiet et al., 2000). The pungency of volatile anesthetics may contribute to the breath-holding seen in birds when an anesthetic mask is placed over their faces.

In ducks isoflurane has a minimum anesthetic concentration of 1.3% (Ludders et al., 1990). In birds, it causes dose-dependent reduction in spontaneous ventilation that extends to apnea at high concentrations (Ludders et al., 1990). The calculated Anesthetic Index (anesthetic concentration causing apnea/minimal anesthetic concentration) for ducks (1.65) is lower than for dogs (2.51), cats (2.40), and horses (2.33) (Ludders et al., 1990, 1995; Steffey et al., 1977; Steffey and Howland, 1977). The lower Anesthetic Index for ducks indicates hypoventilation occurs at lower isoflurane concentrations than in other species. In Pekin ducks isofluraneinduced tachycardia and hypotension (Goelz, 1990). Although arrhythmias were uncommon, one duck died when ventricular bigeminy and multifocal ventricular rhythms progressed to ventricular fibrillation (Goelz, 1990). In other avian species arrhythmias, cardiac irritability and premature ventricular contractions have also been observed (Ludders et al., 1988a, 1989a; Matthews et al., 1991; Aguilar, 1996; Greenlees et al., 1990; Jaensch et al., 1999; Naganobu and Hagio, 2000; Langlois et al., 2003; Straub et al., 2003). Once waterfowl have stabilized under isoflurane anesthesia cardio-pulmonary variables should be carefully monitored (Table 23.3).

Induction

Inhalant anesthetics are administered through a mask for induction. Commercially available cat or dog masks are used for small ducks and geese. Shorebirds may require custom masks fashioned from tubing or syringe cases to accommodate their long bills. The mask must include the nares at the base of the upper bill. The mask aperture can be altered with a piece of surgical glove stretched over the opening, taped around the edges, and with a slit cut into the center. The apnea and bradycardia that occur when an induction mask is placed over a bird's beak and face are commonly attributed to a "dive response," but are owing to a stress response caused by stimulation of trigeminal nerve receptors (Butler, 1988; Jones et al., 1988; Woakes, 1988). Pre-oxygenating ducks with 100% oxygen for several minutes reduced this response in dabbling, but not diving ducks (Furilla and Jones, 1986).

The isoflurane vaporizer is set to 3% to 4% for induction. Although it is recommended the concentration be slowly increased to prevent breath holding, this author has found this ineffective. In ducks and geese the oxygen flow rate is 1 to 2 L/minute to allow relatively rapid changes in anesthetic concentration as vaporizer setting is altered. A system for scavenging or venting waste anesthetic gases is used for safety (Altman, 1992; Mason et al., 1998). Alternatively, for portable anesthetic machines a canister filled with activated charcoal is used. However, not all cartridge brands work equally well (Smith and Bolon, 2004). The charcoal canister is always laid on its side to avoid blocking the bottom vents, causing unwanted back-pressure on the nonrebreathing circuit. If apnea is prolonged during induction, respiration is encouraged by lifting the bird at the base of the wings, then gently pressing its body down on the table. Inflation and deflation of the reservoir bag is used to monitor breathing and ventilation, assuming the mask is snugly fitted against the face of the bird. Anesthetic depth is judged by pulling out a wing or a foot and releasing it. A conscious bird will withdraw either into the folded position. When the bird is assessed unconscious, oxygen flow is turned to zero. It is preferable to turn the oxygen flow on and off (stopping flow of anesthetic through the vaporizer) than to turn the vaporizer down and then back up again (during which time isoflurane vapor continues to flow through the dead space and into the room).

Intubation

Except for very brief procedures, all birds are intubated and ventilated. Waterfowl and shorebirds generally have

long necks, allowing for a long endotracheal tube. Since the syrinx is inside the thoracic inlet, the length of the neck is used to measure the maximum endotracheal tube length.

Some male waterfowl have a bulbous expansion of the trachea and some geese and swans have tracheal loops that lie in the caudal cervical area or within the thorax (McLelland, 1989b). The avian trachea is 2.7 times as long and 1.29 times as wide as the trachea of a similarly sized mammal (McLelland, 1989a). Consequently the anatomical dead space is about 4.5 times that of a mammal (McLelland, 1989a). The increased dead space is compensated for by a low respiratory frequency, about one-third that of mammals. This results in minute tracheal ventilation of about 1.5 to 1.9 times that of mammals (McLelland, 1989a). However, respiration is depressed under general anesthesia, causing a larger percentage of minute ventilation to be devoted to dead space.

Birds have complete endotracheal rings and cuffless endotracheal tubes are preferred to prevent trauma. However, careful use of cuffed endotracheal tubes has been suggested to obtain a good seal (Curro, 1998). Overinflation of a cuffed endotracheal tube may cause a longitudinal rupture of the tracheal rings that is not obvious for 5 to 7 days after intubation, until healing of the lesion and fibrotic narrowing of the tracheal lumen occur (Ludders, 1998). A Cole endotracheal tube is appropriate for very small birds or chicks and ducklings, to prevent passing the tube too far into the trachea. The appropriate diameter of endotracheal tube must be chosen for the species of bird, and its gender and age. An estimate of the external tracheal diameter is made by palpating the throat. In waterfowl, females may require one-half to one full size larger endotracheal tube than males of the same species. In this author's experience all ducks and geese can be intubated and ventilated with 2- to 4-mm (internal diameter) cuffless tubes. Because of the comparatively long necks found in most waterfowl and shorebird species, over-intubation is a problem only with small species or immature birds. However, care is always taken to avoid striking the syrinx with the end of the endotracheal tube.

Except for birds with very long bills and small oral openings, intubation of waterfowl and shorebirds is relatively easy. The glottis is positioned at the base of the tongue and easily seen in most species. In some a dorsal-ventral septum (*crista ventralis*) is present just inside the glottal opening. If a tube cannot be readily passed through the glottis into the trachea, a tube with a smaller outside diameter is used.

For intubation the upper and lower bills are held agape with the fingers of one hand while inserting the endotracheal tube into the glottis with the other (Figure 23.5). Alternatively, in large or long-billed birds an assistant holds both bills, so the person intubating can use one hand to pull the tongue forward while passing the

Seaman et al., 1994 Wilson and Pettifer, 2004 Rode et al., 2003 Ludders et al., 1990 et al., 1990 Goelz et al., 1990 Reference Valverde HCO_3 30 ± 1 24 ± 1 16-27**Table 23.3A.** Mean cardiopulmonary values given as mean with SD (±) or range (−) for waterfowl after at least 15 minutes under isoflurane anesthesia. PaCO₂ (mmHg) 94 ± 12 43 ± 4 32-54 24 $Pa0_2$ (mmHg) 74.4 ± 12.4 348 ± 18 315-433 102 7.17 ± 0.05 7.37 ± 1.05 7.23-7.40 7.42 рНа Mean BP (mmHg) 101 ± 2 119 ± 17 103 ± 11 121 ± 11 95-105 Diastolic BP (mmHg) 75 ± 5 Systolic BP (mmHg) 140 ± 7 Body Temperature (°C) 40.0 ± 0.6 41.3 ± 0.2 41.1 ± 0.2 37.2-37.5 Resp. Rate (BPM) 11 ± 1.6 10 ± 2 22 ± 6 6 ± 1 3-8 10 227 ± 42 190 ± 70 283 ± 23 180-220 Heart Rate (BPM) (Anas platyrhynchos) Pekin duck canadensis (Canada Mallard duck goose) Pekin duck Pekin duck Pekin duck Species Branta

Machin and Caulkett, 1999 Reference et al., 2003 Rode HCO_3 24 ± 1 $PaCO_2$ (mm Hg) 40 ± 3 40 ± 5 **Table 23.3B.** Mean cardiopulmonary values given as mean with SD (\pm) or range (-) for waterfowl after at least 15 minutes under injectable anesthesia. PaO_2 (mm Hg) 83 ± 8 84 ± 12 7.40 ± 0.04 7.34 ± 0.02 pHa 124 ± 13 Pressure (mmHg) 173 ± 24 Blood (mm of Hg) 164 ± 25 Diastolic Pressure Blood Pressure (mmHg) Systolic Blood 186 ± 24 Body Temperature (°C) 40.9 ± 0.4 38.7 ± 0.9 Respir. Rate (BPM) 17 ± 4 31 ± 5 239 ± 16 218 ± 32 Heart Rate (BPM) Propofol (15 mg/kg IV induction; 0.8 mg/kg/ min infusion (160 mg/kg IV) Pento-barbital Anesthetic duck (*Aythya* valisneria) Canvasback Pekin duck (Anas platyrhy-nchos) Species



Figure 23.5. Bristle-thighed curlew (Numenius tahitiensis) being intubated. The left hand is used to hold the upper and lower bills apart, while the right hand inserts the endotracheal tube. It is sometimes easier to intubate long-billed birds by holding the head dorsal side down, which permits the slight curve of the endotracheal tube to follow the curve of the beak. (Photograph courtesy of Dan Ruthrauff.)

endotracheal tube with the other. Endotracheal tubes are usually inserted without lubrication.

Correct tube position is confirmed by direct visualization of the tube in the glottis, condensation on the inside of the tube, and chest excursions during mechanical ventilation. It is a good habit to immediately confirm proper placement by palpating the throat of the bird. If the tube is within the trachea, only one hard tubular structure, the trachea, will be felt ventral to the cervical vertebral column. If the tube was inadvertently passed into the esophagus, two hard tubular bodies will be felt, and corrective action can be immediately taken. The endotracheal tube is secured in place by tying or taping to the lower bill. Since the glottis is located on the ventral oral cavity, taping the tube to the upper bill would allow for movement of the glottis independent of the tube, which may cause inadvertent extubation.

After intubation the anesthetic system is reconnected and oxygen flow restarted to restore isoflurane flow. The vaporizer setting is reduced to maintenance. Anesthetists must ensure the bird's head and neck are in extension to prevent kinking of the endotracheal tube. They must also be alert for gurgling sounds and exaggerated respiratory movements indicative of a blocked endotracheal tube. The use of a mechanical ventilator may reduce the likelihood of endotracheal tube blockage (Kramer, 2002).

The minimal anesthetic concentration (MAC) is relatively constant (about 1.5%) for most species. Many birds will be apneic following induction. It is prudent to use a lower vaporizer setting initially to slightly reduce

anesthetic depth and to restore spontaneous ventilation. A decision to lighten anesthetic depth following induction is accompanied by attention to the anesthetic status of the patient to prevent sudden motion.

Ventilation

Most surgical procedures are performed in dorsal recumbency. This position can cause profound respiratory alteration. In conscious chickens placed in dorsal recumbency tidal volume decreased 40% to 50% although breathing frequency increased by 20% to 50% (King and Payne, 1964). King penguins (*Aptenodynes patagonicus*) injected with tiletamine-zolazepam were immobilized about 50% longer if held in dorsal compared with ventral recumbency, and body temperatures were also significantly higher (Thil and Groscolas, 2002). Respiratory compromise may be worsened in waterfowl by the inertial resistance of the relatively large pectoral muscle mass to respiratory excursions of the keel. The pressure of viscera on the abdominal air sacs also reduces their effective volume.

Inhalant anesthetics cause a dose-dependent depression of spontaneous ventilation (Ludders et al., 1988b, 1989a, 1990; Ludders, 1992). Intermittent positive pressure ventilation is used in anesthetized birds, even if some spontaneous breathing is continuing, to assure adequate oxygenation of the blood (Edling et al., 2001). In geese, an average PaCO₂ of 53 mmHg was necessary for spontaneous respiration to occur; no respiration occurred with a PaCO₂ less than or equal to 40 mmHg (Pizarro et al., 1990). Ventilation is assisted manually using the reservoir bag on the breathing system or a mechanical ventilator (Carpenter and Mason, 2001; Hernandez-Divers, 2001; Pettifer et al., 2002). Analysis of blood gases showed effective gas exchange is achieved using mechanical ventilation (Piiper et al., 1970, 2002; Ludders et al., 1989a; Edling et al., 2001; Mitchell et al., 2001).

Although a decrease in mean arterial blood pressure is observed in mammals during positive pressure ventilation, in sandhill cranes (*Grus canadensis*), pigeons (*Columba livia*), and Amazon parrots (*Amazona ventralis*), blood pressures increased or were maintained during ventilation (Ludders et al., 1989a; Pettifer et al., 2002; Wilson and Pettifer, 2004). However, blood pressure decreased in positive pressure-ventilated chickens anesthetized with sevoflurane (Naganobu et al., 2003). The cardiovascular effects of positive pressure ventilation in birds are still uncertain, and have not been examined in waterfowl and shorebirds.

A spontaneously breathing bird is given greater than or equal to 2 assisted breaths per minute. If an anesthetized bird is apneic the assisted ventilation rate is greater than or equal to 8 to 15 breaths per minute depending on size (large birds require fewer breaths than small birds). If pulse oximetry and capnography are used to monitor respiration the rate is guided by

the end tidal CO_2 level and the relative hemoglobin saturation (Figure 23.3).

OXYGEN AND ANESTHESIA

Inhalant anesthetics depress spontaneous ventilation (Ludders et al., 1988a, 1989a, 1990; Goelz, 1990). It is essential to avoid hypoventilation during anesthesia because birds lack the respiratory reserve capacity to compensate. Oxygen within air sacs does not diffuse into the blood to any great extent (Magnussen et al., 1976).

Using oxygen to deliver inhalant anesthetics to birds can alter respiratory variables. Respiratory rate decreased (but not significantly) as the fraction inspired oxygen increased to more than 90% (Seaman et al., 1994). Increasing oxygen concentration above 40% decreased tidal volume, a decrease that was significantly correlated with arterial CO₂ (Seaman et al., 1994). High oxygen concentrations may depress ventilation by acting on O₂-responsive chemoreceptors (Ludders et al., 1995). The use of ambient oxygen concentration during avian anesthesia would not depress the O₂-sensitive chemoreceptors and have a less depressive effect on ventilation.

Air Sac Cannulation

Air flow through the lung is continuous and unidirectional. Therefore, it is possible to ventilate and to provide anesthesia through an air sac cannula (Whittow and Ossario, 1970; Jaensch et al., 2001; Rode et al., 2003; Brown and Pilny, 2006). A common application of this technique is in patients with tracheal obstructions (Mama et al., 1996; Clippinger and Bennett, 1998; Rode et al., 2003; Graham, 2004). The abdominal air sacs are generally used (Good et al., 2001). The clavicular air sac has been used, but it appears to participate less in ventilation than the thoracic and abdominal air sacs (Jaensch et al., 2002; Rode et al., 2003). Cannulation of the caudal thoracic air sac has been used to anesthetize zebra finches (Taeneopygia guttata) as small as 10 g (Nilson et al., 2004). The technique could easily be adapted for anesthesia of very small ducklings and shorebird chicks.

Placing an air sac cannula requires the selected site (on the lateral abdominal wall well ventral to the spine so as to avoid damage to the kidney) be prepared as with any surgical site. Feathers are taped aside and the skin is prepped. Although general anesthesia makes placement easier, in conscious birds the surgical site is infiltrated with lidocaine (less than or equal to 2 mg/kg). The skin is incised with a scalpel blade. The muscle layer is penetrated with either sharp dissection by making a puncture with a blade or by blunt dissection using hemostats to work through the muscles and air sac membrane. The cannula, often an endotracheal tube, is pushed into the air sac. The tube is secured by suturing tape butterfly wings to the skin. The breathing system is then connected and the animal ventilated. Waste anesthetic gases exit through the trachea and are an exposure risk

to personnel. The cannula is removed when spontaneous ventilation is reliable. Sutures or surgical glue are used to close the incision.

Ducks anesthetized with phenobarbital and breathing room air through clavicular air sac cannulas had no significant differences in arterial blood gas values compared with ducks that were tracheally intubated (Rode et al., 2003). Caudal thoracic air sac cannulation in sulfur-crested cockatoos (*Cacatua galerita*), anesthetized with isoflurane in 100% oxygen, provided adequate blood oxygenation and maintained tidal and minute volumes (Jaensch et al., 2001). However, clavicular air sac cannulation did not provide adequate ventilation or anesthetic maintenance (Jaensch et al., 2001).

PARENTERAL ANESTHESIA

Parenteral anesthesia has several advantages over inhalant anesthesia, including ease of use, rapid onset, minimal equipment, reasonable cost, and minimal contamination of the work space with toxic chemicals. Like inhalants, parenteral anesthetics produce dose dependent cardiopulmonary depression. Few parenteral anesthetics are reversible; once injected they cannot be adjusted and most require renal or hepatic biotransformation to be cleared. Other potential disadvantages include interspecies and individual differences, the need to determine body weight for accurate administration, and a relatively narrow margin of safety. In waterfowl most parenteral anesthetics are delivered into the pectoral muscles, although the large leg muscles can be used.

Empirically derived dosages for parenteral drugs are only available for a few avian species. Alternatively, allometric scaling is used to approximate effective dosages. However, allometrically derived drug dosages in new species should be used with caution (Dorrestein and Van Miert, 1988; Dorrestein, 1991). Allometric scaling can be used to estimate respiratory variables in birds (Frappell et al., 2001). Monitoring of cardiopulmonary variables is essential when using parenteral anesthetics (Table 23.4).

Tiletamine/Zolazepam

Tiletamine/zolazepam has been used both as an injectable and as an oral immobilizing drug in birds, especially larger animals (e.g., ratites, raptors, cranes, and penguins) (Van Heerden and Keefen, 1991; Howard et al., 1993; Kreeger et al., 1993; Lin and Ko, 1997; Lin et al., 1997; Janovsky et al., 2002; Thil and Groscolas, 2002). This combination is rarely used in waterfowl because it does not provide adequate analgesia for painful procedures. In Pekin ducks (*Anas platyrhynchos*) tiletamine/zolazepam (13 mg/kg IM), with lidocaine (100 mg) infiltrated into the skin and musculature at the incision site, was used for anesthesia to surgically collect liver biopsies (Carp et al., 1991).

(Mulcahy et al., 2003)

(Wilberg, 2005)

0.05g IM

Buprenorphine

Pre-anesthetic

Pekin duck

sedation

3.4 IM

Ketoprofen

implantation

Transmitter

Common eider

(Somateria mollisima)

spectabilis)

(Mulcahy et al., 2003) (Mulcahy et al., 2003) (Valverde et al., 1990) (Ludders et al., 1989) Livingston, 2002) Rode et al., 2003) Caulkett, 1998a) (Blogg et al., 1998) (Blogg et al., 1998) Manlove, 2001) (Carp et al., 1991) Caulkett, 1999) (Greenacre, 1993; Pettifer, 2004) Pettifer, 2004 (Wilson and) (Machin and (Machin and (Machin and (Wilson and (Hepp and (mg/kg) Route Reference 0.06 IM 0.05 IV 0.06 IM 0.05 IV0.05 IV Additional Drug Buprenorphine Buprenorphine Medetomidine Medetomidine Medetomidine 100 mg infiltrated (mg/kg) Route 1 IM 11V 21V 2IV2IVSecond Drug Butorphanol Midazolam Midazolam Midazolam Lidocaine Xylazine 0.8 mg/kg/min 15 IV induction; (mg/kg) Route infusion 0.25 IV9-10 IV 2.0 IM 160 IV 5.4 IM 2.2 IM $13 \, \mathrm{IM}^{\mathrm{a}}$ 10 IV 20 IV $20 \, \text{IV}$ 10 IV 2 IM 10 IV 5 IM 1 IV Cis-atracurium Pento-barbital Primary Drug Zolazepam Midazolam Midazolam Tiletamine-Ketoprofen Ketoprofen Ketoprofen Ketamine Ketamine Ketamine Ketamine Ketamine Xylazine Propofol Propofol abandon ment implantation Neuromuscular implantation Pre-anesthetic Sedation for blockade Prevent nest **Transmitter** Liver biopsy radiology **Pransmitter** sedation Anesthesia Anesthesia Anesthesia Anesthesia research Anesthesia research research research research Surgery Purpose Surgery (Aythya fuligula) Canvasback duck platyrhynchos) Spectacled eider platyrhynchos) Canada goose (Aix sponsa) canadensis) Mallard duck Mallard duck Mallard duck Mallard duck (Somateria (Somateria valisneria) Tufted duck Pekin duck Wood duck Pekin duck Pekin duck Pekin duck King eider (Aythya fischeri) (Branta (Anas Species

Fable 23.4. Injectable drugs used in waterfowl.

(Samour et al., 1984) Caulkett, 1998b) Caulkett, 2000) (Cooke, 1995) (Machin and (Machin and (mg/kg) Route Reference Dosage 3 IV 1 IV 0.03 IV 0.05 IV Additional Drug Medetomidine Medetomidine Xylazine Xylazine Xylazine (mg/kg) Route 2 mg/kg IM 0.025 IM $0.025\,\mathrm{IM}$ Dosage 0.05 IM 0.3 IM 0.4 IM 0.1 IM $0.1\,\mathrm{IM}$ 0.2 IM 20 IM 10 IM 36 IM 2 IM 2 IM 1 IM 18 IV 20 IV 40 IV 40 IV 50 IV 20 IV 10 IV 10 IV 10 IV 10 IV 1 IM 5 IM Alphadolone Alphadolone Medetomidine Medetomidine Medetomidine Medetomidine Medetomidine Medetomidine Medetomidine Medetomidine Methohexital Alphaxalone-Alphaxalone-Second Drug Butorphanol Bupivacaine Midazolam Sufentanil Ketamine Ketamine Ketamine Ketamine Ketamine Ketamine Fentanyl Fentanyl Ketamine Ketamine (mg/kg) Route 1-2 mg/kg IV bolus induction; 10 mg/kg IV 3.0-4.2 IV Dosage 8 IM 8 IM 8 IM 8 IM 8 IM 2 20 IM 5 IM 5 IM 5 IM $0.1\,\mathrm{IM}$ 20 IM 24 IM 10 IM 20 IM 5 IM 2 IM 2 IM 8 IM 5 IM 5 IM 1 IV 11 IV 2 IV 5 IV 1 IV 1 IV 2 IV 2 IV 2 IV Alphadolone Alphaxalone-Primary Drug Midazolam Ketamine Xylazine implantation Transmitter Sedation for handling Anesthesia research Induction Purpose Canvasback duck Hawaiian goose (Cygnus olor) Muscovy duck Mallard duck Mallard duck moschata) Mute swan (Calrina (Branta Species

sandvicensis)

 Table 23.4.
 (Continued)

									(Machin and	Livingston, 2002)
						5 IM	10 IM	5 IM		
						Xylazine	Xylazine	Xylazine		
23 IM	11 IM	3 IM		8 IM	51 IM	20 IM	70 IM	20 IM	5 IM	
Alphaxalone- Alphadolone	Alphaxalone- Alphadolone	Alphaxalone- Alphadolone	Xylazine	Xylazine	Xylazine	Ketamine	Ketamine	Ketamine	Ketoprofen	
									Analgesia	research
Mallard duck	Muscovy duck	Hawaiian goose	Mallard duck	Muscovy duck	Muscovy duck	Mallard duck	Muscovy duck	Hawaiian goose	Mallard duck	

 $^{\rm a}\!Additional$ doses of 3 mg/kg were used to extend an esthesia.

Ketamine

Ketamine alone is not used in waterfowl and shorebirds because of poor muscle relaxation and spontaneous movement, even at high dosages. It is often combined with other drugs to minimize these unwanted side effects. In Pekin ducks xylazine alone (1 mg/kg IV) or combined with ketamine (20 mg/kg IV) induced hypoventilation and hypoxemia (Ludders et al., 1989b). In Pekin, mallard, and tufted ducks (*Aythya fuligula*), a combination of ketamine (10 mg/kg IV), midazolam (2 mg/kg IV), and medetomidine (0.05 mg/kg IV) was effective for anesthesia and surgery (Blogg et al., 1998; Machin and Caulkett 1998b).

α₂-Adrenergic Agonists

Xylazine/ketamine combinations were commonly used for avian field anesthesia. Xylazine has largely been replaced by medetomidine. In mallards IV, but not IM, medetomidine/midazolam/ketamine produced adequate analgesia and anesthesia for a 30-minute period (Machin and Caulkett, 1998a). In the same study, various combinations of medetomidine, ketamine, fentanyl, midazolam, butorphanol, methohexital, or alphaxalone-alphadolone delivered IM or intranasally were either ineffective in producing more than moderate sedation or lethal. Medetomidine and xylazine, alone or in combination with other drugs, are used with caution. Sometimes they fail to immobilize birds or else they produce significant cardiopulmonary side effects (Sandmeier, 2000; Pollock et al., 2001; Atalan et al., 2002; Uzun et al., 2003; Varner et al., 2004). An advantage to the use of α_2 -agonists alone or in combination with other drugs is their reversibility with the α_2 -antagonists, atipamezole and yohimbine.

Local Anesthetics

Lidocaine and bupivacaine, both lipophilic amino amides, are most commonly used. Their duration of effect has not been determined in birds, but in mammals lidocaine lasts 1 to 2 hours and bupivacaine 4 to 6 hours (Skarda, 1996; Lemke and Dawson, 2000). Use of local anesthetics in birds has been limited by fear of toxicity. To avoid adverse side effects (i.e., depression, drowsiness, seizures, and cardiovascular collapse) the maximum dose is precalculated (4 mg/kg lidocaine, 2 mg/kg bupivacaine) (Hocking et al., 1997; Machin, 2005a). Vasoconstrictors (i.e., epinephrine) have been added to lidocaine solutions to slow systemic absorption and extend the duration of action. However, when a longer duration of action is desired, a longer acting drug (e.g., bupivacaine) should be chosen instead.

Propofol

Propofol has found increasing popularity in waterfowl anesthesia. It can be used for induction followed by an inhalant for maintenance (Goulden, 1995). Although not a widely used technique in birds, propofol can be

administered by a constant rate infusion. Canvasback ducks (*Aythya valisneria*) were maintained with a constant rate infusion (0.8 mg/kg per minute) following a bolus induction (15 mg/kg) (Machin and Caulkett, 1999). More commonly it is given by bolus, both to induce and maintain anesthesia, and the frequency and size of the boluses are titrated to maintain the desired anesthetic depth. Propofol has a narrow therapeutic index. Artificial ventilation may mask overdosage because the initial sign of toxicity is hypoventilation (Machin and Caulkett, 1999). With waterfowl and shorebirds apnea should be expected in all individuals given propofol (Mulcahy, unpublished data).

Alphaxalone/Alphadalone

A mixture of alphadolone acetate (3 mg/mL) and alphaxalone (9 mg/mL) has found limited use in waterfowl. This combination has been used for induction and as a sedative for handling (Samour et al., 1984; Cooke, 1995; Machin and Caulkett, 1998b).

VASCULAR ACCESS

The veins most commonly used for vascular access are the jugular, medial metatarsal, and basilic. For both waterfowl and shorebirds, the jugular vein is used to obtain blood samples of greater than or equal to 1 ml and can be used for placement of relatively large catheters. The jugular is the largest peripheral vein, has a fairly thick wall and hematoma formation is uncommon. The right jugular vein is often stated to be larger than the left, but either is used.

The basilic vein crosses the medial distal humerus and, because it is visible under the skin, is a favorite phlebotomy site for the inexperienced. However, its narrow lumen, thin walls and curving course make it difficult to obtain more than a small blood sample. In small birds, it can be pierced with the needle tip and a few blood drops collected using capillary tubes. Hematomas occur very commonly, because of its thin wall and poor technique. Their formation is prevented in several ways. First, place pressure over the needle and vein prior to withdrawing the needle, preventing blood leakage. Second, place just enough pressure to reduce blood flow, but not to empty the vessel. If the latter occurs, a hematoma forms when the pressure is lifted and blood rushes back into the vein and out the puncture. Finally, place gentle pressure over the puncture site for greater than or equal to 2 minutes to allow adequate clotting.

The medial metatarsal vein courses along the medial aspect of the tarsometatarsal bone and crosses the tibiotarsal joint. The presence of scaly skin may increase the level of discomfort for the bird when this site is used. However the vein is usually visible, the featherless skin permits good disinfection, and the tightness of the skin discourages hematoma formation. Blood is obtained using the needle-nick technique, a needle and syringe,

or a butterfly catheter. The relatively small diameter of the vein minimizes the amount of blood that can be obtained, especially in small birds. However, it is useful for administration of drugs, including propofol. Although clotting at this site is usually not a problem, clotting enhancers can be used.

ANALGESIA

In waterfowl and shorebirds, any procedure that would cause pain in humans or result in tissue damage should be performed under anesthesia with consideration for analgesia (see Chapter 3). However, species differences in response to analgesics, and the relative paucity of published research in waterfowl, makes selection and dosing difficult. Preemptive administration of analgesics is more effective, as it is in mammals, in easing the pain caused by tissue damage during surgery.

Non-steroidal Anti-inflammatory Drugs (NSAIDs)

Flunixin meglumine, ketoprofen, and carprofen have all been used in waterfowl. Flunixin meglumine is not recommended because of a greater risk of adverse effects than in mammals (Clyde and Paul-Murphy, 1999). These effects, noted in other bird species, include renal toxicity, regurgitation, tenesmus, and injection site necrosis (Mansour et al., 1988; Clyde and Paul-Murphy, 1999; Machin et al., 2001; Machin, 2005a). Nonsteroidal drugs that are not selective for cyclooxygenase-2 are used with caution. In male eiders, the nonselective NSAID ketoprofen was implicated in renal toxicosis and death when given perioperatively (Mulcahy et al., 2003). Female eiders were not adversely affected. This sex related difference was thought to be due to physiologic changes associated with male behavior on the nesting grounds. Ketoprofen (5 mg/kg IM) takes about 30 minutes from injection to the onset of analgesia (Machin and Livingston, 2002).

Birds eliminate NSAIDs rapidly, but differences in elimination rates occur between species (Baert and De Backer, 2003). Compared with chickens, ostriches (*Struthio camelus*), turkeys (*Meleagris gallopavo*), and pigeons (*Columba livia*), ducks (*Anas platyrhynchos*) are intermediate in elimination half-life for meloxicam (0.72 hours), an NSAID selective for cyclooxygenase-2 (Baert and De Backer, 2003).

Opioids

Opioids have generally been avoided in waterfowl because of fear of respiratory depression. Birds differ from mammals in their response to mu agonist opioids. This appears to be owing to a preponderance of κ opioid receptors over μ (Mansour et al., 1988). Butorphanol (1 mg/kg) combined with midazolam (2 mg/kg) was used as premedication for isoflurane anesthesia in a mallard duck (Wilson and Pettifer, 2004). Buprenorphine

(0.05 mg/kg, IM) given to domestic ducks 1 hour before induction with isoflurane, effectively reduced reaction to painful stimuli, but had strong respiratory depressant effects (Wilberg, 2005). In tufted ducks buprenorphine (0.06 mg/kg IM) was given at the time of anesthetic induction to provide post-surgical analgesia (Blogg et al., 1998). Premedication with butorphanol (1 mg/kg IM) or morphine (0.1 to 3.0 mg/kg IV) allows a dosedependent reduction in inhalant anesthetics in chickens (Concannon et al., 1995) and in a psittacine (Curro et al., 1994), but not turkeys (Reim and Middleton, 1995). In harlequin ducks (*Histrionicus histrionicus*) preanesthetic administration of butorphanol (0.5–2.0 mg/kg IM) did not reduce isoflurane requirement for surgery (Mulcahy, unpublished).

FIELD TECHNIQUES

Free-living waterfowl and shorebirds are anesthetized for a variety of reasons, including restraint. Laparoscopic sexing was a common indication (Risser, 1971; Fiala, 1979; Greenwood, 1983; Garcelon et al., 1985; Ketterson and Nolan, 1986; Richner, 1989). However, unless immediate results are needed, surgical sexing has largely been supplanted by molecular techniques (Griffiths, 2000; Boutette et al., 2002). An increasing number of field anesthesias and surgeries are done to collect liver biopsies for determination of cytochrome P450 1A, a hepatic enzyme induced by exposure to hydrocarbons from spilled oil (Trust et al., 2000; Esler et al., 2002; Golet et al., 2002; Jewett et al., 2002; Peterson et al., 2003). Isoflurane is the anesthetic of choice for taking surgical liver biopsies from birds (Degernes et al., 2002). The cytochrome P450 isoenzyme responsible for the limited isoflurane metabolism is different from that assayed for oil spill exposure (Kharasch and Thummel, 1993).

There is a growing need for avian field anesthesia to surgically implant transmitters and data loggers (Butler and Woakes, 1979; Olsen et al., 1992). Many waterfowl species, especially diving birds, do not tolerate external attachment of transmitters. Implanted transmitters are better tolerated, but signal strength is greatly attenuated. An important advance in the technique has been the addition of percutaneous antennas that solved the signal attenuation problem (Korschgen et al., 1996). Percutaneous antennas also allowed recently miniaturized satellite transmitters (PTT-100, Microwave Telemetry, Columbia, MD) to be implanted in waterfowl, especially sea ducks (Petersen et al., 1995, 1999, 2003, 2006). Coelomically implanted transmitters are placed in an abdominal air sac, but no studies have evaluated the respiratory effects of a large foreign body in this air sac.

Complicating the anesthesia required to implant transmitters into the air sacs is the surgeries are often done in remote locations in tents, on boats, or even inside helicopters (Brown and Luebbert, 2002). The opening of part of the respiratory system to the atmosphere carries its own complications. In spontaneously breathing pigeons anesthetized with isoflurane, the opening of an air sac for endoscopic splenic biopsy worsened hypoventilation, despite an increased respiratory rate (Touzot-Jourde et al., 2005). This response was possibly due to high PaCO₂ or to a lighter anesthetic plane following dilution with room air entering the incision. If the birds were ventilated mechanically, the ventilator did not achieve the selected inspiratory pressure due to leakage through the open air sac. In those birds a respiratory alkalemia developed and PaCO₂, HCO₃, base excess, heart rate, and mean arterial blood pressure were all significantly decreased, although PaO₂ was maintained (Touzot-Jourde et al., 2005). The incision required to implant a transmitter creates a much larger opening in the abdominal air sac than does that for an endoscopic biopsy. This suggests the cardiovascular effects during implantation are the same or worse.

When free-living birds require general anesthesia it is rarely possible to do more than a quick physical examination preinduction. The ability to do hematology and serum chemistries is usually not available. The emergence of point-of-care blood analyzers eventually will permit at least some prescreening, and even consumergrade blood glucose analyzers have begun to be used in seabird rehabilitation (Lieske et al., 2002). The prandial status of wild avian anesthetic candidates is usually unknown, and it is advisable to hold wild birds for as short a time as possible, to limit stress. It is recommended to hold birds for about an hour before anesthesia, to prevent intra-operative draining of crop contents with subsequent aspiration.

Holding, Transportation, and Handling

In field research surgical facilities are usually centralized and the birds transported by truck, boat, aircraft, or by being hand-carried from the capture site. Birds are transported in soft bags, boxes, or animal carriers. Cardboard boxes are rarely suitable because of the lack of air circulation, even if holes are punched through the sides. Techniques for carrying birds are directed at protecting them from trauma, minimizing stress, and preserving the protective function of the feathers. It is preferable to transport birds individually, to prevent fighting. If more than one bird must be placed in a transport container, mixing birds of the same sex is avoided.

The size of the container should be sufficient to allow the bird to stand and turn around. Shorebirds especially prefer standing, and it may be detrimental to place them in a container that prevents them from doing so. Placing a number of birds into a larger container is not recommended; the birds generally huddle in the back of the container and will not use the extra space. If too many birds are placed into a single container, trauma or death from suffocation may result from birds piling up in a corner.

The insulation of feathers and aquatic lifestyle of waterfowl contribute to hyperthermia during dry transportation. This author has seen body temperatures as high as 43.9°C at induction in birds that later survived anesthesia and surgery. A transport container must have adequate ventilation to prevent hyperthermia. Commercial cat and dog crates have grated windows which let air circulate (Figure 23.6). However, the grid may permit bird bills to pass through and suffer damage. This is especially important when holding long-billed shorebirds. The existing grid is covered with finer mesh netting that prevents trauma, but still allows air circulation and observation of the bird.

Prevention of feather soiling during transportation and holding is very important. Soiled feathers are a source of infection during surgery, and are less capable of maintaining a constant body temperature during anesthesia and recovery. Following release, a soiled bird has to devote more time to preening. This leads to



Figure 23.6. Examples of holding and recovering cages made by modifying an animal carrier by the addition of artificial turf (top) or mesh surrounding a PVC-pipe frame (bottom) to reduce fecal soiling of feathers. A turf bottom (top) is safer for a bird like the bar-tailed godwit (Limosa lapponica), that has a long bill and toes, to reduce the chance of entanglement. A finer mesh net should be attached to the inside of the wire-grid door and air holes to prevent damage to bills of shorebirds and ducks such as the common eider (Somateria mollissima), shown in the bottom picture.

increased energy expended, reduced feed consumption, and increased risk of predation. A towel or other absorbent material is placed on the bottom of the transport container. If the bird is permitted to rest directly on the bottom of the container, the towels are changed frequently to assure a clean and dry substrate. It is preferable to have waterfowl and shorebirds rest on netting suspended from a frame on the bottom of the container (Figure 23.2). The mesh size should be small enough to prevent toe entanglement, but allow excreta to pass through. Alternatively, artificial turf is used for the substrate (Figure 23.2).

When captured, wild birds rarely eat or drink in transport or temporary holding facilities, especially with humans nearby. Pretreatment holding times are, therefore, limited to less than or equal to 1 to 2 hours to prevent excess stress and dehydration. For most procedures, birds are returned to their holding containers for about an hour after they have recovered, then released.

The feathers are often disarranged or damaged during capture and initial handling to free the bird from nets or traps. Handling must be gently done to maintain feather integrity and waterproofing, especially for waterfowl that will be released into cold waters. If surgery is done on wild-caught water birds intended for immediate release, feathers are not be plucked because it increases heat loss into cold water following release. It also imposes an increase in energy demand during feather replacement. Instead of plucking, the feathers are swept clear of a surgical site and held to the side with a water soluble "liquid bandage" (e.g., Facilitator, IDEXX Pharmaceuticals, Greensboro, NC). The covering feathers are held apart to expose the down and a line of liquid bandage is placed on them and massaged in. The liquid bandage collapses the structure of the down feathers, allowing them to be swept to the side, exposing the skin. The liquid bandage quickly becomes tacky, holding the collapsed down to the sides. The cleared surgical field is minimal, but is sufficient to allow an incision. Since it is water soluble the liquid bandage is quickly preened free of the feathers within hours of the bird's release. Honey has been used to in lieu of liquid bandage in field work (Cheryl Scott, personal communication). Tape (Micropore Surgical Tape, 3M Health Care, St. Paul, MN) can be applied to the feathers wetted with liquid bandage to further prevent contamination of the surgical site. A transparent sterile barrier drape (Veterinary Specialty Products, Mission, KS) with an adhesive backing will stick to the tape and following the procedure, both can be peeled off with minimal feather loss.

In field anesthesia of wild birds lingering sedative effects are undesirable. Birds are released relatively quickly after recovery from anesthesia, placing them at risk of injury or predation or unable to maintain social status in a flock or a pair bond commitment. Because of these risks, analgesics that might compromise reactivity (e.g., opioids) are not used.

Field Anesthesia

Oral Drug Administration Waterfowl and other birds have been captured using bait treated with α -chloralose, a centrally active chloral derivative of glucose (Belant and Seamans, 1997, 1999; Bailey et al., 1999; Belant et al., 1999). Other oral drugs used to capture waterfowl have not had the same level of use and experimentation (Cline and Greenwood, 1972). α-Chloralose is a soporific and narcotic; it does not produce general anesthesia. It has been most used as an avicide to control nuisance birds. Although usually added to corn, it has also been combined (30 mg/kg) with margarine and used in tablet form to capture Canada geese (Branta canadensis) (Crider, 1967; Belant and Seamans, 1997). This approach is used for birds that habitually use a certain area. When applied to a substrate like bread, individual birds can be targeted if they can be approached and thrown the bait. However, induction is very long and recovery may take many hours. As a result, this drug is not suitable for birds that are to be quickly released after a procedure. Multiple exposures may be complicated by drug accumulation in the tissues.

α-Chloralose is hazardous to use and a current Material Safety Data Sheet must be obtained from the manufacturer and consulted for the proper personal protective equipment. Legal use of α -chloralose in the United States requires an Investigational New Animal Drug Application (#6602) issued by the Food and Drug Administration to the Animal and Plant Health Inspection Service, US Department of Agriculture. In mallard ducks the effective dose (ED₅₀) is 15 mg/kg and the lethal dose (LD₅₀) is 34 mg/kg, resulting in a therapeutic index (TI = LD_{50}/ED_{50}) of 2.2 (Cline and Greenwood, 1972). α -Chloralose is much less safe in mallard ducks than chickens where $ED_{50} = 45 \text{ mg/kg}$, $LD_{50} = 300 \text{ mg/kg}$, and TI = 6.7 (Loibl et al., 1988). This difference indicates that interspecies variability in susceptibility must be carefully considered. Overdosing is a potential problem; birds that have ingested α -chloralose are at risk of drowning if they enter the water. Drugged birds that escape and die in wetlands are a slight risk for starting an outbreak of avian botulism in waterfowl (Goldberg et al., 2004). Care is taken to prevent secondary poisoning of non-target species, including domestic animals (Segev et al., 2006).

Other drugs have been added to bait, but none are registered for use as veterinary drugs. Although tiletamine-zolazepam (80 mg/kg PO) caused deep sedation of common buzzards (*Buteo buteo*), this combination has not been evaluated in wild waterfowl (Janovsky et al., 2002).

Inhalation Anesthesia

Inhalation anesthesia in free-living birds is usually performed with isoflurane. The minimum equipment for administration includes a tank of oxygen, regulator and pressure tubing, flow meter, vaporizer, and breathing system (see Chapter 5). Most people prefer the vaporizer

and flow meter mounted on a stand for convenience. Concepts of portability vary, and a "mobile" anesthesia apparatus to anesthetize 150-g doves might be one that fits snugly into the back of a truck (Small et al., 2004).

Use of compressed oxygen in the field at low ambient temperatures may contribute to loss of body heat. If safely possible oxygen cylinders are kept in a warmed environment. Exposure to very cold temperatures can shrink metal parts and seals causing gas leakage. This author has had oxygen cylinders fresh from refilling plants prove to be empty after transportation to very cold field sites. Cylinder valves transported to cold environments are tightened more than usual and checked upon arrival at the field location. It is prudent to always have a plan for an alternative anesthetic technique (e.g., injectable drugs).

Induction of wild-caught waterfowl is done using isoflurane and a mask. The vaporizer is set at 4% with a minimum oxygen flow of 1 L/minute for most ducks and small geese. Occasionally a wild bird is sufficiently stressed to resist induction and the vaporizer is turned to 5%. If induction resistance occurs regularly, consideration should be given to pre-medicating the birds.

Intranasal Drug Administration Intranasal administration of sedative drugs has seldom been used in avian anesthesia. In mallard ducks intranasal alphaxalonealphadolone had no effect (Machin and Caulkett, 1998a). Intranasal ketamine, midazolam, methohexital, and butorphanol alone or in combination produced light sedation at best, as did intranasal ketamine and midazolam when combined with IV propofol (Machin and Caulkett, 1998a). However, intranasal delivery was not combined with isoflurane administration. Intranasal midazolam or diazepam sedated canaries (Serinus canarius) and ring-necked parakeets (Psittacula krameri) sufficiently that they tolerated dorsal recumbency, while xylazine and detomidine caused sedation (Vesal and Eskandari, 2006; Vesal and Zare, 2006). The effects took only 1 to 2 minutes to occur. The antagonist drugs flumazenil and yohimbine were also successfully used via the intranasal route. The same agonists can be given IM as pre-anesthetic sedatives, but onset of action will not be as fast. Flumazenil should not be given IM. The rapid onset and duration of action of sedatives given intranasally to birds warrants further attention for use in reducing stress in captured wild birds intended for anesthesia and surgery.

Hazardous Material Shipping

Inhalant anesthetics and compressed oxygen cylinders are classified as hazardous materials for air transportation and can only be shipped as cargo, never as checked baggage (Anon., 2006). Failure to follow regulations governing shipment of hazardous materials may result in significant legal sanctions. They must be shipped in specific packaging, with appropriate hazard labels and

forms. Hazardous materials shipping agents should be consulted to assure proper packaging and labeling. Adequate time and planning must be allowed to assure the anesthetic and oxygen will arrive when needed. Additional regulations apply to moving hazardous materials on other forms of public transportation (e.g., buses, trains, and ferries) and via transportation corridors such as tunnels and bridges. Empty oxygen cylinders are not classified as hazardous materials and may be transported on passenger aircraft. To avoid confusion and delay, empty oxygen tanks and their packaging should have all hazardous materials labels removed or covered. It is prudent to leave the valves of empty cylinders open during shipping to avoid partial re-pressurization owing to temperature or air pressure changes, and to attach a large label stating "Empty" to the container.

Properly packaged and labeled isoflurane and other inhalant anesthetics can be shipped (as cargo) on an aircraft bearing passengers, but compressed oxygen cylinders can only be carried on purely cargo flights. In some cases it may be possible to transport isoflurane, but not compressed oxygen to a field site because of the types of aircraft services available to the nearest staging area. If medical-grade oxygen cannot be shipped to a location, a large tank regulator can be fitted to a tank of welder's oxygen, which can often be found in remote villages and on commercial fishing boats. Alternatively, it is possible to drive an anesthetic vaporizer using compressed air. A small electric air compressor and a low pressure, 22-L portable air tank such as those used by house painters to power paint sprayers can be shipped to the field as baggage without concern for Hazardous Material shipping regulations. Most field camps have small electrical generators for recharging batteries. The air tank is filled using the air compressor and then is connected to a flow meter and thence to the vaporizer (Figure 23.7). The air pressure in the tank should not fall below 0.34 Mpa (50 psi), limiting this technique to short duration procedures unless the compressor is run continuously. It is theoretically possible to fill the air tank using a hand driven bicycle tire air pump, assuming sufficient enthusiasm for prolonged physical exertion. Specialized draw-over vaporizers, developed for battlefield use, use air and have been adapted for use in wild animals (Lewis, 2004). With any inhalant anesthetic system using air it is critical to provide adequate ventilation to assure oxygenation.

Injectable Anesthesia

Given the difficulties of transporting inhalant anesthetics and compressed oxygen cylinders, it is not surprising injectable anesthetics have been assessed for their usefulness in field surgeries. In waterfowl propofol has been used as a general anesthetic, combined with bupivacaine or a 2:1 mixture of bupivacaine/lidocaine infused at the incision site, for the intra-coelomic implantation of radio transmitters (Machin and Caulkett, 1999,



Figure 23.7. Assembly of an air-driven inhalant anesthetic system that drives a vaporizer with compressed air from a low-pressure, small volume air tank filled by an electrical air compressor.

2000). The propofol/bupivacaine anesthetic system eliminates shipping hazardous materials. In addition, the equipment required for propofol/bupivacaine is much less expensive, and the mass of materials required is a fraction of that required using isoflurane as an anesthetic (Figure 23.8).

The author has used propofol and bupivacaine/ lidocaine in field surgeries exclusively for several years to implant transmitters into hundreds of birds with good results. The medial aspect of the tibiotarsus is prepared for catheter placement by cleaning and disinfecting with non-detergent iodophor solution. A 0.508-mm (25-gauge), 1-cm butterfly catheter (No. 4573, Abbott Laboratories, North Chicago, IL) is placed in the medial metatarsal vein (Figure 23.9). Stability of the catheter is improved by snipping the plastic butterfly wings from the needle. Since propofol should be administered slowly, this size catheter can be used on a wide range of body sizes of birds. Birds are induced by slow administration of propofol (20 mg/kg or to effect, depending on the temperament and level of excitement of the bird). Following induction, which occurs within seconds, the catheter and its tubing are taped in place. Following preparation of the surgical site, bupivacaine or bupivacaine/lidocaine mixture (2:1 v/v) is infused at and around the incision site to a maximum of 2 mg/kg. Additional propofol is given by bolus (1-4 mg/kg) to maintain a plane of anesthesia suitable for the procedure being done. Clues to indicate the need for additional propofol are movement or tone in the legs and wings, or opening of the eye with the presence of a reflex movement of the nictitating membrane.

Anesthesia to Prevent Nest Abandonment

Waterfowl sitting on nests while laying or incubating eggs are commonly captured for marking with tags or transmitters, measuring or sampling. The stress of removing a sitting bird and the presence of humans when the bird is replaced on the nest causes a high rate



Figure 23.8. Comparison of equipment and supplies required to perform an identical number of surgeries using isoflurane (left) or propofol (right). The latter system totals about 10% of the weight of the former. The cartons containing the oxygen cylinders bear Hazardous Materials labels.



Figure 23.9. A 0.508-mm (25 ga), 1-cm butterfly catheter placed in the tibiotarsal vein of a yellow-billed loon (Gavia adamsii) and connected to a syringe holding propofol. The wings of the "butterfly" have been cut off to reduce the chance of dislodging the needle.

of nest abandonment. Briefly anesthetizing gray partridges (*Perdix perdix*) and mallards being returned to the nests on which they had been captured almost eliminated nest abandonment (Smith et al., 1980; Rotella and Ratti, 1990).

Despite widespread use, it is considered inappropriate and hazardous to use any inhalant anesthetic by pouring it onto cotton balls (Heard, 1997). Methoxyflurane is placed on cotton in a container at the nest site; the head of the bird is then placed into the container until muscle relaxation occurs. The bird is then placed on the nest with its head tucked under its wing and the researcher quickly withdraws. The bird is

closely monitored to prevent anesthesia becoming too deep because no vaporizer is used. A light anesthetic depth is sufficient because the bird only needs to be obtunded for the length of time it takes to place it on the nest and withdraw. When methoxyflurane manufacture was discontinued in the 1990s some biologists switched to isoflurane delivered via cotton ball to birds being replaced on nests. However, the properties of isoflurane make it more hazardous than methoxyflurane to use for this purpose.

Propofol has recently been used to render birds unconscious to prevent nest abandonment (Machin and Caulkett, 2000; Hepp and Manlove, 2001). Propofol (10 mg/kg over one min followed by additional 1 to 2 mg/kg boluses until induction) is delivered via a catheter in the medial metatarsal vein (Machin and Caulkett, 2000).

Induction of wood ducks ($Aix\ sponsa$) with methoxyflurane averaged 5 minutes; although not stated it is presumed that wood ducks given propofol IV were immediately induced (Hepp and Manlove, 2001). There was no significant difference in mean time to recovery for wood ducks anesthetized with methoxyflurane (11.8 ± 1.6 minutes) compared with propofol (9.2 ± 0.8 minutes) (Hepp and Manlove, 2001). The disadvantage of using propofol is that the biologist must be able to deliver it into a vein at the nest site. An advantage of propofol is that it is not classified as a hazardous material for the purpose of shipping.

Mention of trade names does not imply government endorsement.

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24

Ratites

Jessica Siegal-Willott

INTRODUCTION

Ratites belong to the avian orders Struthioniformes (ostriches), Casuariformes (emus and cassowaries), Rheiformes (rheas), and Apterygiformes (kiwis) (Smith, 2003). Depending on the classification system, Tinaniformes (tinamous) may also be included.

Taxonomy and Biology

Ostriches (*Struthio camelus*) are the largest living birds (Table 24.1). There are several recognized subspecies confined to Africa and portions of the Middle East. Ostriches are sexually dimorphic; males are generally larger and have distinctive black feathers and wing plumes.

The common (*Rhea americana*) and Darwin's or lesser (Rhea pterocnemia) rhea are endemic to the grasslands of South America. The emu (Dromaius novaehollandiae) is confined to Australia. Emus are second in size to the ostrich, with the females slightly larger than males. There are three cassowary species, the double-wattled (Casuarius casuarius), single wattled (Casuarius unappendiculatus), and the Dwarf cassowary (Casuarius bennetti), all native to the Australasian rainforests. The three species of kiwi are confined to New Zealand; the great spotted (Apteryx haastii), the little spotted (A. owenii), and the brown (A. australis). Tinamous are small flighted ground dwelling birds from the forests of South America. There are 47 recognized species and they are either classified as, or are considered the closest avian relatives to the ratites described in the preceding.

Anatomy and Physiology

The term ratite refers to the flat raft-like sternum lacking a keel bone for attachment of the large flight muscles. All have elongated necks and relatively long, muscular legs, but little pectoral muscle development. All possess elongated toenails for aggression or defense, and are strong and rapid runners. Ostrich toenails are blunted, whereas those of other ratites are sharp. Rheas can

abruptly change direction when running, and both rheas and cassowaries are powerful swimmers.

As with other birds, ratites lack a diaphragm. They possess much reduced air sacs compared with flighted birds. Respiration requires movement of the sternum down and forward, with the ribs expanding outward. This is inhibited when weight, such as from a person straddling the bird, is applied from above. Death of birds thus restrained has been attributed to hypoxemia. Only the femur is pneumatized in ostriches and emus (Fowler, 1996).

The normal respiratory rate of an adult ostrich is 6 to 12 breaths per minute (bpm), but may increase up to 40 to 60 bpm during periods of hyperthermia. Normal body temperature (38°C–40°C) is maintained during thermal stress using evaporative cooling from the trachea, air sacs, and pharynx (Fowler, 1996). The ratite glottis is simple with a large opening, an adaptation proposed to facilitate inhalation of air during strenuous exercise (Figure 24.1). The trachea is composed of complete cartilaginous rings.

Ratites possess a renal-portal system, similar to other birds. Although theoretically it might enhance excretion of renally eliminated drugs, in ostriches administered xylazine/tiletamine/zolazepam there was no significant difference between injection in the thigh or muscles at the base of the wings in onset, duration, or recovery (Carvalho et al., 2006). The physiologic role of the renal-portal system is poorly understood; care is used when potentially nephrotoxic drugs or those primarily eliminated by the kidneys (i.e., ketamine) are administered into the thigh musculature or medial metatarsal vein.

The ostrich is the largest living bird, with some males weighing as much as 160 kg (Table 24.1). Both male and female emus possess a ventral midline tracheal sac, approximately 10 to 15 cm cranial to the thoracic inlet.

The kiwi nares are located close to the beak tip; this location is thought to facilitate scent location of food among forest leaf litter. The kiwi egg is the largest proportionately of any living bird. Prior to oviposition it

Table 24.1. Reported weight and height ranges for ratites and tinamous.

Species	Height	Weight		
Ostrich	2.1-3.0 m	$\leq 160 \text{ kg}^a$		
Emu	1.5-1.9 m	30-55 kg ^b		
Cassowarys				
Double wattled	1.3-1.7 m	♂ 29-34 kg		
Single wattled	1.5-1.8 m	♀ ≤58 kg		
Dwarf	1.0-1.1 m	NR		
Rheas				
Greater	1.2-1.7 m	20-25 kg ^a		
Darwin's	1.0-1.1 m	10-25 kg ^a		
Kiwis	0.35-0.55 m	0.67-4 kg ^b		
Tinamous	NR	$0.04-2.3 \text{ kg}^{\text{b}}$		

NR = Not reported; a = males larger than females; b = females larger than males.

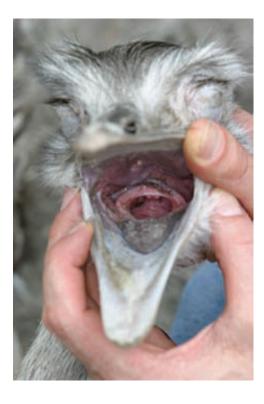


Figure 24.1. The glottis of most ratites, as in this rhea, is large and readily visible at the base of the tongue.

occupies a large proportion of the coelomic cavity with a consequent reduction in air sac space. Further compromise to respiration owing to pulmonary compression occurs if the animal is turned on its back. Kiwis also have lower body temperature (36.6°C–40.3°C) and metabolic rate than most other birds (Smith, 2003).

PHYSICAL RESTRAINT

Young ratites (chicks and small juveniles) weighing less than or equal to 6 kg are manually restrained by supporting under the body and allowing the legs to hang or be folded. Birds weighing 6 to 15 kg are restrained with a hand around the abdomen, leaving the legs free. Care is taken during catching or handling to prevent damage to the legs. Chicks can also be wrapped in a towel for restraint or travel.

Juveniles and adult ratites require experienced handlers for restraint. These birds are large and strong, and possess large claws on the toes often used for defense. Emus and cassowaries in particular have large nails on the medial digit. Male ostriches are especially dangerous during the breeding season. Ratites jump, kick, and slash in a forward direction, and thus are approached from behind or the side to minimize risk of injury to the handler. Emus can also kick sideways, and rheas can kick in any direction. Gloves and protective clothing are often useful in preventing trauma from the distal limbs during restraint. Assuming a flat (prone) position on the ground will prevent trauma from kicking if escape from the bird is not possible.

Physical restraint of adult ratites by experienced handlers involves straddling the bird, with its legs in front of the holder. The wings should be grasped at the level of the humerus; the bird may also be restrained by a hand over the breast plate. Emus should not be restrained at the humerus, as the wings are reduced in size and may fracture. Emus accustomed to handling, and gently restrained from behind, may allow collection of blood or injection of anesthetics into the right jugular vein. However, the bird will respond violently if the upper neck or head is grabbed.

Alternatively, in ostriches the head may be grasped and quickly lowered below the level of the body. This prevents the ratite from kicking above its head level, minimizing the risks to the handler. This method of restraint is often used to place a hood, and possibly injection of medications.

Padded chutes, boards, alleyways, and stanchions are useful in the movement, separation, and isolation of individual animals for restraint and anesthetic procedures. Dim lighting (emus, rheas, cassowaries, ostriches) and/or hooding (ostriches only) to decrease visual stimuli are useful for restraint. Hoods should cover the eyes without occluding the nostrils, and extend approximately one-third of the distance down the neck (Cornick-Seahorn, 1996) (Figure 24.2). Hooks are not recommended for catching or restraint as they may result in lacerations of the neck and/or trachea, and possibly death of the bird if not used appropriately (Raines, 1998). However, in some situations this is the only way to catch the head for hood placement. Proper construction and application of hooks are described by Fowler (1995).

Emus present special challenges. Their skin is thin and easily lacerated. The head and long neck are vulnerable to injury because of the lack of significant muscle or soft tissue covering. The trachea is also easily collapsed. These birds are readily stressed, with subsequent respiratory or



Figure 24.2. A hood reduces excitement and struggling in ostriches; it is not recommended in other ratites.

circulatory collapse, exertional rhabdomyolysis (see Chapter 11), self-trauma, and hyperthermia (see Chapter 10). Lastly, emus are capable of jumping high distances (less than or equal to 2 m), and will attempt escape. Juvenile emus are more tractable requiring only an experienced handler. One hand is placed between the legs and on to the sternum, leaving the other hand free to immbolize the head and neck (Mouser, 1996).

Cassowaries are aggressive, requiring sedation or anesthesia for most handling procedures; hooding or covering the eyes is not adequate for safe restraint. During the very short period of sexual receptivity, captive females may be approached and allow examination and blood collection.

If possible, physical restraint occurs in secure areas, with solid, non-slip surfaces, free of large, deep water sources, obstacles that may injure the bird or handler (hooks, nails, ledges, holes, wire, machinery, etc.), and at a suitable ambient temperature. Capture enclosures are designed to minimize risks to the patient and handlers, with easily accessible exit routes. Padded equine recovery stalls, with lights that can be dimmed, are excellent areas for restraint, induction, and recovery. Heavy foam pads, when used as shields, protect handlers and are used to compress birds in a confined space for IM or IV injections. These pads are cleaned and disinfected between uses.

VASCULAR ACCESS

Intravenous injections and phlebotomy are performed using either the right jugular (14–22 g), brachial, or

medial metatarsal vein. The medial metatarsal vein is not accessible in the awake adult. In emus the basilic vein is small (although still able to be catheterized) as a result of vestigial wing development. The wings are also prone to fracture during manual restraint (Cornick-Seahorn, 1996).

Intravenous fluids are administered to anesthetized ratites at 5 to 10 ml/kg per hour. Fluids commonly used include lactated Ringer's solution, Ringer's solution, and 0.9% sodium chloride. Fluid supplementation with dextrose may be warranted in young and/or debilitated birds. If IV access is not possible, intraosseous (IO) catheters may be placed in juvenile birds. The ulna and tibiotarsus are commonly used for IO access (see Chapter 23).

ENDOTRACHEAL INTUBATION

Non-cuffed endotracheal (ET) tubes are used to prevent pressure necrosis of the tracheal mucosa, although some authors prefer cuffed tubes to minimize the risk of aspiration and ensure effective mechanical ventilation. The glottis is large and easily visualized for insertion of the ET tube (Figure 24.1). Light bandaging around the neck of emus prevents air from distending the subcutaneous air sac during positive pressure ventilation.

The head and neck are positioned to prevent kinking of the ET tube, and minimize risk of regurgitation and aspiration. Tube internal diameter varies with bird size, ranging from 4 to 18 mm. Intubation and positive pressure ventilation are recommended for all prolonged (greater than or equal to 10 minutes) or surgical procedures. Ventilatory support aims to achieve a tidal volume of 10 to 20 ml/kg, respiratory rate of 6 to 12 breaths per minute, and a peak inspiratory pressure of 10 to 15 cm water (Cornick-Seahorn, 1996; Fowler, 1996).

ANALGESIA

Use of analgesics is based on experience in other avian species (see Chapters 3 and 23). Limited work has been done to establish dosage ranges in ratites. Fentanyl and butorphanol have been used as adjuncts to general anesthesia for pain control (Cornick-Seahorn, 1996).

CHEMICAL RESTRAINT AND ANESTHESIA

Drugs used for chemical restraint in ratites are summarized in Table 24.2. Intramuscular administration is routine; the cranial and caudal thigh muscles and lumbosacral area (in non-obese birds) are used, since the pectoral muscles are not developed. The role of the renal-portal system in drug elimination following administration into caudal musculature has not been fully elucidated. Intravenous drug administration offers the most rapid method of immobilization; in intractable animals, IM sedation may be required prior to IV access.

 Table 24.2.
 Anesthetic agents used in adult ratites.

Agent	Ostrich	Emu	Rhea	Cassowary	Comments	Reference
Sedation						
Azaperone	0.5-2					Jensen, 1990
	0.55					Gilsleider, 1998
Detomidine	1.5			4 401		Jensen, 1990
Diazepam	0.05			1 q18 h	Γ	Tully, 1996
	0.3-0.5				For recovery	Smith, 2003; Cornick-
	0.1-0.2a					Seahorn, 1996 Cornick-Seahorn, 1996
	$0.1-0.2^{\circ}$ $0.1-0.3^{\circ}$					Ramsey, 1991
	$0.1-0.3$ 0.3^a					Gilsleider, 1998
	0.33 ^{a,b}					Lin, 1997
	0.5-1	5 ^{a,e}	5 ^{a,e}			Cornick-Seahorn, 1996
	5 ^e PO					Fowler, 1995
Medetomidine	0.1					VanHeerden, 1991
	0.26-0.31				Light sedation	Westcott, 2002
	0.38-0.54				Heavy Sedation	Westcott, 2002
Medetomidine/				0.09-0.13/	Heavy sedation	Citino ^g
Ketamine				$3.4-4.3^{b}$		
Medetomidine,				0.12-0.13	1st dart	Citinog
Medetomidine/				$0.04/0.2^{b}$	2nd dart combo	
Midazolam	0.154					6 1 1000
Midazolam	0.15 ^d 0.15 ^{a,b}					Cornick, 1992
Telazol/	0.15	3.3/0.13 ^b				Lin, 1997 Tully, 1996
Diazepam		3.3/0.13				Tully, 1996
Xylazine	0.2-2					Gilsleider, 1998
Ay luzific	0.4-0.9					Cornick, 1992
	0.5-1					Fowler, 1995
Xylazine/Butorphanol			2.26-2.75/			Lin, 1997
			0.12-0.2			,
Immobilization						
Carfentanil	3.3 ^e					Fowler, 1995
Carfentanil/Ketamine	3/200 ^e					Fowler, 1995
Carfentanil/				0.04-0.06/	Stormy induction	Citino ^g
Midazolam/				0.1-0.2/	possible	
Ketamine				$2.5 - 4.9^{h}$	-	
Etorphine	1.5-6 ^{e,i}					Fowler, 1995
Etorphine/	2.5-3/50 ^{b,e}				Variable	Stoskopf, 1982
Acepromazine	3.6/15 ^{b,e}				Excitement Mode-	Samour, 1990
T. 1. /	5 10 T 10 0 0 0				rate sedation	4000
Etorphine/	6/25/200 ^e					Samour, 1990
Acepromazine/						
Xylazine				0.1/6.55	Dorrosso	Englary 1004
Etorphine/Ketamine				0.1/6.55 (ket) ^c	Reverse	Ensley, 1984
				(Ket)	etorphine with diprenorphine	
	2-6e/150-200e			7-12 ^e /	Long, smooth	Stoskopf, 1982
	2 0 /130 200			100-300e	recoveries	5.05корт, 1502
Etorphine/	8-9/4-8 ^{e,i}			100 300	recoveries	
Medetomidine	,					
Medetomidine/	$0.08/2^{\rm b}$				Bradycardia	Langan, 2000
Ketamine	0.05-0.15/3-7				•	Fowler, 1995
Metomidate/	20/6.6 ^b				Apnea;	Van Heerden, 1991
Azaperone	10/3.3 ^b				respiratory side	
					effects; salivation	
					regurgitation at	
T. 1 1	5 ach				higher dose	17 11 1 1001
Telazol	5-20 ^b					Van Heerden, 1991
Xylazine	1-2.2					Jensen, 1992
						Fowler, 1995
Induction						0.11
Alphaxalone/	2.41–4.8 ^a					Cullen, 1995
Alphadolone						

 Table 24.2.
 (Continued)

Agent	Ostrich	Emu	Rhea	Cassowary	Comments	Reference
Carfentanil	0.03 ^d 0.3				Poor induction;	Honnas, 1991 Cornick, 1992
Diazepam/Telazol Diazepam/Ketamine	0.1/4.4 0.22/4.4 ^{a,d} 0.2-0.3 ^a /2-10 ^a 0.1/8				арпса	Cornick-Seahorn, 1995 Honnas, 1991 Gilsleider, 1998 Fowler, 1995
	0.22ª/4.4ª				Bradycardia; Hypercapnia; poor induction	Cornick, 1992
Isoflurane Ketamine/Xylazine/ Guaifenesin	5%	5% 15/3/ 0.1% K/ 0.05% X/ 5	5% % G		Juveniles (<6 mo) Induce with K/X; maintain on K/X/ G IV at 2–4 ml/ kg/hour	Cornick-Seahorn, 1996
Propofol	3 ^b 0.2 mg/kg/min ^f				Apnea may occur	Langan, 2000 Langan, 2000
Telazol	3.7 ^a 3.7 ^a				Poor/rough recovery; apnea	Honnas, 1991 Cornick, 1992
	2.3–4.9 ^a 4.35	2.3-4.9 ^a	2.3-4.9 ^a		After sedation with diazepam	Lin, 1997 Tully, 1996
Xylazine/ Alphaxalone/	5 1.13-1.85/				•	Gilsleider, 1998 Cullen, 1995
Alphadolone Xylazine/ Butorphanol/ Telazol	1.66-3.53 ^a 1.06-2.03/ 0.10-0.14/ 2.3-4.0 ^a	1.06-2.03/ 0.10-0.14/ 3.4-4.9 ^a	2.12-2.75/ 0.12-0.55 3.0-5.8a	/	Higher doses needed in rheas	Lin, 1997
Xylazine/ Carfentanil	0.5/0.015 ^a 0.5/0.15 ^a ,d 150 mg ^e /3 mg ^e	3.1-1.7	3.0-3.0		Apnea Reverse with yohim bine/naltrexone	Honnas, 1991 Cornick, 1992 Raath, 1992
Xylazine/Diazepam/ Ketamine	0.44/0.15/2.8 ^d				bilic/flattexoffe	Honnas, 1991
Xylazine/Diazepam/ Ketamine	0.44/0.15 ^a / 2.8 ^a				Poor induction	Cornick, 1992
Xylazine/Ketamine	0.45/25 2.2/2.2-3.3 0.5-1/2-10 a					Matthews, 1991 Fowler, 1995 Gilsleider, 1998
Xylazine/Ketamine/ Alphaxalone- alphadolone	1/5/12-17.1 ^{a,b}				Supplemental A-A needed for pro- longed procedures	Gandini, 1986
Analgesia Butorphanol	0.02 0.02-0.05 ^a					Cornick-Seahorn, 1995, 1996
Reversals Atipamezole Diprenorphine	5–20 ^{a,e} 2x etorphine			2x etorphine		Ostrowski, 1995 Stoskopf, 1982
Naltrexone	dose (mg) 90–125 mg:1 mg			dose (mg)		Raath, 1992
Yohimbine	carfentanil 0.11					Lin, 1997
Emergency Drugs Atropine Doxapram	0.035 5 ^a					Fowler, 1987 Ostrowski, 1995 Cornick-Seahorn, 1996
Epinephrine Glycopyrrolate Lidocaine	0.02-0.2 ^a 0.011 ^a 1-2 ^a				For ventricular arrythmias	Cornick-Seahorn, 1996 Cornick-Seahorn, 1996

Doses are based on mg/kg basis. All agents administered intramuscularly (IM) unless stated otherwise.

^aIntravenous administration; ^bJuvenile animal; ^cSupplemental drug needed on mg/kg basis; ^dSupplemental isoflurane needed for intubation; ^cTotal mg per bird; ^fConstant rate infusion of propofol used to maintain a light plane of anesthesia in juvenile ostrich; ^gPersonal communication; ^hSupplemental ketamine needed for transportation; ⁱFree ranging; G = guaifenesin; K = ketamine; X = xylazine.

Fasting times vary based on age and size of the bird, with little to no fasting in those less than 6 months old to prevent hypoglycemia. Adult ratites are fasted for 12 to 24 hours prior to induction (Cornick-Seahorn, 1996; Lin et al., 1997).

Chemical immobilization is conducted in safe, secure areas with escape routes available for all personnel involved. Successful chemical immobilization varies with age and species, as well as experience level of the handlers and anesthetist(s).

Premedications

Anticholinergics are not commonly used, as they increase the viscosity of respiratory secretions, potentially leading to airway obstruction (Gilsleider, 1998). Bradycardia is not commonly encountered during ratite anesthesia. In ostriches, anticholinergic therapy is indicated if heart rate falls below 30 to 35 bpm (Cornick and Jensen, 1992). However, anticholinergic therapy is not consistently effective in treating bradycardia (Cornick and Jensen, 1992). Many instances of bradycardia are likely owing to hypertension and therefore are refractory to anticholinergics.

Tranquilization and sedation have been achieved using acepromazine, azaperone, diazepam, midazolam, xylazine, detomidine, ketamine, and medetomidine, allowing for blood collection, minor procedures, and facilitation of induction of anesthesia (Table 24.2). These medications are usually administered IM; oral diazepam has been used successfully to sedate ostriches and cassowaries (Fowler, 1995; Kapustin, personal communication).

Xylazine is commonly used, either alone or in combination with ketamine. Caution is warranted when using this α_2 -agonist, as it has significant cardiorespiratory depressant effect. Onset of action is usually within 10 minutes, and may provide up to 30 minutes of sedation (Gilsleider, 1998). Low-dose medetomidine allowed for safe approach and limited handling in adult captive and free-ranging cassowaries, and was fully reversed with atipamezole administration (Westcott and Reid, 2002). Higher doses produced heavy sedation adequate for full examination (Westcott and Reid, 2002). Juvenile (less than 1 year) cassowaries were heavily sedated using medetomidine/ketamine combination; degree of sedation was somewhat variable, and supplemental M/K was occasionally necessary for some procedures (Citino, personal communication). Intramuscular medetomidine, followed by medetomidine/midazolam IM in these same cassowaries produced mild sedation adequate for crate-loading (Citino, personal communication).

Acepromazine is useful for muscle relaxation, but is contraindicated in debilitated animals, and is not a preferred method of tranquilization. Safer drugs for healthy and ill birds include diazepam and midazolam. Azaperone is useful for transport of animals, as it provides little muscle relaxation, but adequate tranquil-

ization for up to 24 hours (Cornick-Seahorn, 1996; Gilsleider, 1998).

Immobilization

Opioid Combinations Carfentanil and etorphine have been used with limited and variable success. Carfentanil produces rapid recumbency, but has been associated with excitatory activity (frenzied running, circling, walking backward) (Cornick and Jensen, 1992; Citino, personal communication). In severe cases this excitatory phase results in exertional rhabdomyolysis or trauma. Etorphine has been used in combination with acepromazine, acepromazine and xylazine, ketamine, and with medetomidine. In each case satisfactory muscle relaxation and sedation were achieved, and use of medetomidine allowed for complete immobilization. In ostriches etorphine combined with medetomidine produced recumbency in less than 10 minutes in most cases (Ostrowski and Ancrenaz, 1995). Risks with these combinations include regurgitation, aspiration, myopathy, and death (Cornick-Seahorn, 1996).

In juvenile ostriches (less than 1 year) etorphine/ acepromazine had no or variable effect, from mild sedation to profound immobilization. Etorphine/ketamine showed similar but more reliable immobilization and recovery when administered to adult ostriches (Stoskopf et al., 1982). Some of the variability may have been a result of dart failure. Manual restraint was used to assist the adults into sternal recumbency following adequate tranquilization. In contrast, lower dosages of etorphine/ acepromazine administered via blow dart produced moderate sedation for 10 to 20 minutes in juvenile birds, with some ataxia and excitement during the initial immobilization (Samour et al., 1990). In adult ostriches higher dosages of etorphine/ acepromazine, in combination with xylazine, improved sedation and allowed manual restraint for diagnostic procedures. Initial effects were similar to those noted above (Samour et al., 1990). Ostriches appear resistant to high etorphine dosages (Stoskopf et al., 1982; Samour et al., 1990). Given the unpredictable effects of etorphine/acepromazine combinations alternative immobilizing and induction agents should be considered first.

In adult cassowaries etorphine (less than or equal to 10 mg) did not produce immobilization (Stoskopf et al., 1982). However, a combination of etorphine/ketamine produced immobilization within 25 minutes in most birds, but was associated with long, rough recoveries (Stoskopf et al., 1982). A similar etorphine/ketamine combination (6/400 mg) was used to successfully induce a cassowary for surgical removal of a mass (Ensley et al., 1984). This combination produced recumbency within 5 minutes; however, supplemental ketamine was necessary for safe handling and administration of general anesthesia (Table 24.2). Adult cassowaries have been immobilized with a carfentanil/midazolam/ketamine combination. Animals were recumbent within

10 minutes, and occasionally exhibited an excitatory phase. Supplemental ketamine was given in some instances to allow for safe transport (Citino, personal communication).

Other Combinations In ostrich chicks undergoing four different anesthetic combinations, only metomidate/ azaperone IM produced satisfactory anesthesia and analgesia with relatively few side effects (Van Heerden and Kefren, 1991). In the same chicks tiletamine/zolazepam, metomidate, and metomidate/ azaperone IM produced successful immobilization; an adult ostrich given a similar dose of tiletamine/ zolazepam exhibited violent kicking and self-trauma, and insufficient immobilization (Van Heerden and Kefren, 1991). The immobilization times were dosage dependent and most combinations did not fully eliminate voluntary movements. Medetomidine alone (0.1 mg/kg) did not produce immobilization (Van Heerden and Kefren, 1991). In contrast, juvenile ostriches (9-11 months old) were successfully immobilized with a medetomidine/ketamine (0.08 mg/kg; 2 mg/kg) combination, although recumbency was not achieved in all cases (Langan et al., 2000). Tiletamine/zolazepam in combination with diazepam has also been used to immobilize a juvenile emu (Tully et al., 1996).

Induction

In young (less than or equal to 6 months) and easily restrained animals (including kiwis and tinamous) induction may be accomplished using isoflurane alone; large subadult to adult birds require parenteral anesthetics. Inhalant induction is accomplished by starting at a high concentration (such as 5%), then decreasing to maintenance levels. This technique allows for rapid and smooth induction, and is the preferred method for ratites.

A variety of parenteral anesthetics alone or in combination (e.g., xylazine, ketamine, carfentanil, tiletamine/zolazepam, etc.) (Table 24.2) have been investigated and used for induction. Selection is based on age, health status, and species. Known pre-existing disease conditions are also considered.

Opioid Combinations Carfentanil has been used alone and in combination with xylazine for both immobilization and induction of anesthesia (Honnas et al., 1991; Cornick and Jensen, 1992). Common complications include apnea, hypercapnia, excitability, agitation, and frenzied activity (Cornick and Jensen, 1992). Naloxone or preferably naltrexone is used to reverse the effects of carfentanil, and tolazoline or atipamezole may be used to reverse the xylazine, making this a fully reversible combination. The addition of midazolam (0.1 mg/kg) to the C/X combination (0.025/1 mg/kg) allowed for smooth induction and recovery in an adult ostrich; midazolam was not reversed (Citino, personal communication).

Other Combinations. Tiletamine/zolazepam IV produced rapid and smooth induction with sternal recumbency in adult ostriches, and allowed for endotracheal intubation in juvenile ostriches (Honnas et al., 1991; Lin et al., 1997; Gilsleider, 1998). Intravenous administration was facilitated by prior xylazine/butorphanol (X/B) administration in adults; rheas required higher dosages of X/B than emus and ostriches to achieve the same level of sedation (Lin et al., 1997). Despite excellent induction, tiletamine/zolazepam IM is often associated with prolonged "rough" recoveries. These effects are lessened by diazepam before or after tiletamine/ zolazepam administration (Cornick and Jensen, 1992; Tully et al., 1996). Midazolam IM is expected to produce similar effects as diazepam; benzodiazepine administration is encouraged when using tiletamine/zolazepam combinations. Finally, tiletamine/zolazepam IV may result in apnea, necessitating assisted ventilation (Cornick and Jensen, 1992).

Immobilization with medetomidine/ketamine, followed by IV propofol, allowed for safe, smooth induction and recovery of anesthesia in juvenile ostriches (Langan et al., 2000). Transient apnea occurred but spontaneously resolved; all birds were bradycardic throughout the procedure. Light anesthesia was maintained with a constant rate infusion of propofol; higher doses are necessary for a surgical plane of anesthesia (Table 24.2).

Ketamine alone is not recommended due to excitation during induction and recovery, and possible convulsions. Rather, it is combined with other drugs (e.g., diazepam, midazolam, medetomidine, or xylazine) (Cornick and Jensen, 1992; Langan et al., 2000). High dosage diazepam/ketamine and other combinations result in "rough," unpredictable inductions, but smooth recoveries (Cornick and Jensen, 1992). Diazepam (0.3–0.5 mg/kg IM) premedication facilitates induction with ketamine/diazepam IV (Cornick-Seahorn, 1996). Xylazine combined with carfentanil (X/C) or ketamine (X/K) has resulted in successful induction in healthy ratites. However, rough recoveries were noted in some birds with X/K along with bradycardia and apnea (Matthews et al., 1991; Cornick and Jensen, 1992; Fowler, 1995; Gilsleider, 1998). Xylazine/ketamine is not recommended in debilitated birds because of cardiopulmonary depression.

There is considerable variation in effectiveness of anesthetic agents used for induction. This variability may be related to dosage, route of administration, species, age and metabolic rate, or individual variation. In general, diazepam appears to improve induction and recovery regardless of the other drugs used.

Maintenance

Isoflurane is the inhalant anesthetic of choice for chicks and juveniles, and lengthy procedures in adult birds. However, halothane, methoxyflurane, and nitrous

oxide have also been used successfully. Non-rebreathing systems are used in birds less than or equal to 7 kg, with an oxygen flow rate of 200 mL/kg per minute. Circle rebreathing systems are used in larger birds (greater than or equal to 50 kg), with a flow rate of 20 to 30 mL/kg per minute.

Injectable protocols have not provided adequate maintenance anesthesia for prolonged periods. Some success is possible using ketamine and xylazine for induction, followed by IV infusion of ketamine, xylazine, and guaifenesin (Cornick-Seahorn, 1996) (Table 24.2). Repeated IV administration of ketamine (5 mg/kg) at 10- to 15-minute intervals can be used to prolong and/or maintain immobilization (Bruning and Dolensek, 1986).

Intravenous pentobarbital is not recommended, as it has been associated with regurgitation and prolonged recoveries (Cornick-Seahorn, 1996). Propofol may be a useful alternative for extended anesthetic procedures; clinical and research evaluation of its use in ratites is limited, but promising (Langan et al., 2000).

RECOVERY

Birds should be recovered in a dark, quiet, well-padded area to minimize stress and trauma. Use of diazepam (0.13-0.41 mg/kg IV) or midazolam (0.15 mg/kg IV) to produce a calming effect during the recovery period may help minimize self-trauma (Cornick and Jensen, 1992). Alternatively, manual restraint of the bird in sternal recumbency until it is able to stand without assistance can be used. Some clinicians restrain the bird in a towel or tarpaulin using tape or cargo straps until the bird is able to support itself. If this method of restraint is used, quick-release holding straps are recommended. Commercially available wraps are available for use in ratites (Raines, 1998). An alternative method involves recovering the bird in sternal recumbency surrounded by hay bales, with a tent of bales over the top of the bird. The bird is not released from this enclosure until fully alert (Heard, personal communication).

Reversal agents available include yohimbine, atipamezole, naloxone, naltrexone, diprenorphine, and flumazenil (Table 24.2). Reversal agents such as yohimbine for antagonism of xylazine are not commonly employed in ratite anesthesia protocols. Atipamezole is used for reversal of α_2 -adrenergic agonists (xylazine, detomidine, and medetomidine), and flumazenil is used for reversal of the benzodiazepines. Flumazenil is not routinely used because of associated costs and lack of necessity (Cornick-Seahorn, 1996). Intramuscular injection of diprenorphine has been used to reverse the effects of etorphine. Intravenous naloxone administration followed by diprenorphine IM was noted to allow for smoother recovery following carfentanil administration than naloxone alone (Cornick and Jensen, 1992).

In some cases clinicians may prefer intramuscular administration of reversal agents instead of intravascular administration to allow for a more gradual recovery. Extubation is not recommended until the bird is swallowing on its own, and able to maintain its head in a normal position. The oral cavity should be examined prior to extubation to ensure excess secretions, blood, or debris is removed to maintain a clear airway. Re-narcotization has not been reported, but birds should be monitored closely following reversal administration.

FIELD ANESTHETIC TECHNIQUES

There is presently no ideal technique for immobilization or anesthesia of ratites. Field immobilization is complicated by large drug volumes, and "rough" induction and recovery periods. There are also only limited reported investigations of field techniques. Both blowpipes and carbon dioxide powered guns have been used, in combination with plain or barbed darts, for remote drug injection (see Chapter 4). Ideally, reversible anesthetic regimens are used (see Chapter 24).

Administration of medications using darts delivered by CO₂ powered pistol has had mixed success for immobilization of cassowaries and ostriches. Pole syringe use is hampered by difficulty in gaining proximity and access to injection sites (Stoskopf et al., 1982). Blowpipes and non-barbed darts have also been used to deliver drugs to the thigh or lumbosacral muscles (Samour et al., 1990). For successful dart injection a perpendicular trajectory path into the muscle is required. Darts projected at an angle are likely to bounce out of the muscle prior to full delivery of medications (Stoskopf et al., 1982; Samour et al., 1990). Ratites accumulate fat over the pelvis and paralumbar musculature, and in obese captive birds this area is avoided for IM injection.

Evaluation of metodomidate/azaperone in captive ostrich chicks resulted in successful immobilization; although recommended for field use, it was not evaluated in adult ostriches or non-captive settings (Van Heerden and Kefren, 1991). Etorphine and etorphine/medetomidine combinations have been used to capture adult ostriches (Fowler, 1995; Ostrowski and Ancrenaz, 1995). Based on investigations in captive ratites, high dosage ketamine/xylazine combinations may produce field capture and restraint; supplemental IV ketamine is necessary to prolong immobilization (Bruning and Dolensek, 1986).

Carfentanil may cause induction excitement; this is lessened when combined with xylazine (Raath et al., 1992). This combination otherwise produced minimal to no adverse side effects, and was reversed with naltrexone and yohimbine without complication. Carfentanil/ketamine combinations have also been recommended (Fowler, 1995).

Exertional rhabdomyolysis (capture myopathy) may occur in chemically immobilized ratites (see Chapter 10);

field procedures are conducted by experienced personnel and at appropriate ambient temperatures. If excessive stress, excitement, or activity occurs prior to darting, it is prudent to abort the procedure. Medications and supplies necessary for treatment of exertional myopathy should be available during immobilization procedures.

MONITORING

Depth of anesthesia is assessed using heart rate and rhythm, respiratory rate and character, arterial blood pressure, wing and/or neck tone, and assessment of pedal, palpebral, and corneal reflexes. Continuous cardiac monitoring is achieved using an electrocardiogram or manual auscultation. Esophageal stethoscopes are used in chicks or small ratites. The brachial, medial metatarsal or digital arteries are used for pulse assessment. Heart rates of 45 to 80 beats per minute are considered normal in anesthetized adults. The respiratory rate in an anesthetized adult ratite ranges from 25 to 40 (Gilsleider, 1998).

Direct arterial blood pressures are measured by inserting catheters at the arterial sites listed above (Cornick and Jensen, 1992; Lin et al., 1997). Additional arterial sites include the craniolateral aspect of the tibiotarsal bone, and parallel to the mandibular beak within the oral cavity (Cornick-Seahorn, 1996). Based on information from mammalian species, a mean arterial pressure greater than or equal to 60 to 70 mmHg is desirable. However, based on research it is proposed that ostriches normally have a higher arterial blood pressure than mammals (Cornick and Jensen, 1992; Lin et al., 1997). Different drug combinations in different species and age animals are expected to affect the mean, systolic, and diastolic blood pressure; the limited ranges reported in the literature may serve as a rough guideline for acceptable values in ratites (Matthews et al., 1991; Cornick and Jensen, 1992; Lin et al., 1997) (Table 24.3).

Arterial blood gases and pH can also be monitored, although normal values are limited or non-existent.

Additional monitoring includes capnography to assess ventilation, cloacal temperature, and pulse oximetry. The pulse oximetry probe can be applied at the wing web, tongue, or tibiotarsal area. Juvenile birds in particular are susceptible to hypothermia, whereas adults may experience hyperthermia; frequent assessments of the cloacal temperature is recommended.

COMPLICATIONS

Complications associated with physical restraint either pre- or post-anesthesia include: wing fractures, tibiotarsal fractures, tarsometatarsal joint luxation, lacerations caused by hooks or other restraint devices, cervical vertebrae dislocation or fracture, compression injury of the trachea, hypoxemia, peroneal nerve damage, and capture myopathy.

Anesthetic complications noted in the literature include: hypothermia (especially very young and very thin birds), hyperthermia, regurgitation (especially in cases with pre-existing gastrointestinal disease), hypoglycemia, neuropathy and myositis (caused by insufficient padding during anesthesia), tracheal occlusion owing to poor neck positioning, apnea, premature ventricular contractions (cause undetermined; Matthews et al., 1991), bradycardia, cardiac arrest, hypertension (Matthews et al., 1991), voluntary movement, selftrauma during recovery, excessive oral and respiratory secretions, hypocapnia (possibly related to excessive intermittent positive pressure ventilation), hypercapnia (Cornick and Jensen, 1992), secondary fungal/yeast infections (Matthews et al., 1991), and rupture of great vessels (Honnas et al., 1991; Cullen et al., 1995).

Doxapram (5 mg/kg IV) can be used in cases of apnea, and hypotension can be treated using increased IV fluid administration, decreasing anesthetic depth, IV dobutamine (2–5 μ g/kg per minute) or IV dopamine

Table 24.3. Systolic (SBP), mean (MAP), and diastolic (DAP) arterial blood pressures (mmHg) reported for anesthetized ratites.

		S	SBP		MAP		DAP	
Drugs	Species	Minimum	Maximum	Minimum	Maximum	Minimum	Maximum	Reference
X/B	R	68-72	82-120	49-56	60-99	32-51	52-91	Lin, 1997
I	E, R	55-105	121-222	37-84	99-168	30-79	84-147	Lin, 1997
	Ó	102-150	148-198	92-140	142-175	84-128	130-170	Cornick, 1992
	O	145	206	118	171	90	147	Cornick, 1996
TZ	E, R, O	47-178	186-232	44-126	135-210	39-103	122-192	Lin, 1997
X/B/TZ	E, R, O	72-124	131-203	44-80	81-147	36-70	65-124	Lin, 1997
D/K	O	160	254	126	212	85	198	Cornick, 1992
X/D/K	O	162	275	134	232	104	200	Cornick, 1992
X/C	O	160	185	132	158	90	122	Cornick, 1992
X/K	O	136	175	82	105	52	60	Cornick, 1992
	O	168-206	228	108-165	145-191	77-126	120-153	Matthews, 1991
X/K/G	E	99	146	60	109	43	66	Cornick, 1996

B = Butorphanol; C = Carfentanil; D = Diazepam; O = Ostrich; E = Emu; G = Guaifenesin; I = Isoflurane; K = Ketamine; R = Rhea; TZ = Telazol (Tiletamine/Zolazepam); X = Xylazine.

(5 μg/kg per minute). Epinephrine (0.02–0.2 mg/kg IV or intratracheal) can be used in cases of cardiac arrest, in conjunction with cardiac compression applied to the lateral aspect of the bird (Cornick-Seahorn, 1996). Voluntary movement may be avoided by using butorphanol (0.02–0.05 mg/kg IV) to control pain, or by using ketamine intraoperatively (0.2 mg/kg IV). Bradycardia has been arbitrarily defined in the literature as heart rate less than 30 beats per minute. Anticholinergic agents such as glycopyrrolate or atropine have met with variable success in treatment of bradycardia in ratites (Cornick-Seahorn, 1996). Xylazine administration is thought to be associated with bradycardia in ratites, but conclusive evidence is lacking at this time.

Myopathy is treated with supportive care (IV fluids with bicarbonate, dextrose, corticosteroids, vitamin Eselenium, calcium, antibiotics, and flunixin meglumine) and possibly dantrolene for muscle relaxation.

DISEASES OF CONCERN

Procedures requiring general anesthesia in the ratite include: laceration repair, evaluation of traumatic injuries, sequestra removal (Tully et al., 1996), removal of retained or infected yolk sacs, esophagostomy tube placement, pro-ventriculotomy or ventriculotomy for foreign body removal, egg binding, orthopedic procedures (including correction of congenital or acquired musculoskeletal disorders), tumor removal and impaction of the gastrointestinal tract (Ensley et al., 1984; Honnas et al., 1991; Cornick and Jensen, 1992; Gilsleider, 1998). Conditions causing a distended ventriculus or proventriculus (i.e., foreign body) necessitate rapid induction and intubation to minimize the risk of regurgitation and subsequent aspiration (Honnas et al., 1991; Cornick-Seahorn, 1996).

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Section VI Mammal Anesthesia

25

Monotremes (Echidnas and Platypus)

Peter Holz

INTRODUCTION

The monotremes are unique among mammals as they lay shell-covered eggs but nurse their young. There are three species: the short-beaked echidna (*Tachyglossus aculeatus*) found throughout Australia and New Guinea, the long-beaked echidna (*Zaglossus bruijni*) found in New Guinea only, and the platypus (*Ornithorhynchus anatinus*) found along the east coast of Australia.

ECHIDNAS

Short-beaked echidnas weigh between 2 and 7 kg, whereas long-beaked echidnas can weigh up to 10 kg. Their dorsal surface is completely covered in spines, which are firmly attached to the skin and do not pull out the way porcupine spines do.

Capture and Physical Restraint

Echidnas have strong front feet and large pectoral muscles adapted for digging. When approached, the echidna will attempt to bury itself into the ground, rolling into a partial ball with its head tucked under its body, leaving only its spine covered dorsum exposed. Although they do not contain venom, the spines are sharp and will injure the unwary handler. Male echidnas have spurs on their hindlegs. Although sharp, they are not venomous and they do not strike out with their spurs.

To dislodge the semi-buried echidna a spade is required to dig under its body and lift it up. Alternatively a hindfoot can sometimes be grasped. The entire echidna can then be lifted up by the foot and placed in a suitable receptacle, such as a plastic garbage can. Bags are not suitable for holding or transporting echidnas because of their spines.

If the echidna is placed on a solid surface it will attempt to curl into a ball if approached. Again, a hand should be slid under the rear of the body and attempts

made to grasp a foot. Alternatively the entire echidna is picked up either with a towel to protect the hands or wearing sturdy leather gloves. If picking up the echidna by the leg, it is important to be wary of the cloaca, as stressed echidnas frequently spray urine and feces.

Anesthesia

General anesthesia is required for examination because of the echidna's tendency to roll into a ball. As the echidna usually tucks its beak quite tightly into its body it is often not possible to access the beak for mask induction. Consequently the echidna should be placed in an induction chamber connected to an anesthetic machine and flooded with a mixture of isoflurane and oxygen. Once sufficiently sedated the animal is removed, a mask is placed over its nose, and it is maintained with the inhalant anesthetic. Intubation is not possible because of the narrow oral cavity, inability to visualize the larynx, and presence of a keratinous pad on the dorsal surface of the base of the tongue.

Occasionally echidnas are presented wedged into the luggage compartment of automobiles. These echidnas cannot be physically removed and must be induced by injectable agents to remove them from the vehicle. A combination of xylazine (2 mg/kg IM) and ketamine (10 mg/kg IM) works well. This combination can be reversed with yohimbine (0.1 mg/kg IV). A combination of tiletamine/zolazepam (5 to 7 mg/kg IM) has also been reported to be effective (Vogelnest, 1999). Intramuscular injections can be administered into the hindleg, proximal to the stifle.

Vascular Access

On the dorsal surface of the beak, just caudal to the nostrils, lies a soft swelling that represents a venous sinus. This sinus is suitable for blood collection using a 25-gauge needle and 2- to 3-ml syringe. A heparinized winged infusion set (butterfly catheter) will reduce the likelihood of the needle coming out of the sinus if the

echidna moves. Do not exert too much pressure on the syringe, as this will collapse the sinus (Johnston, 2006). The jugular vein can also be used, but is more difficult to access because of the echidna's short neck (Figure 25.1).

Physiology

Normal body temperature is 28°C to 33°C, heart rate is 80 to 110 beats per minute, and respiratory rate is 8 to 14 breaths per minute (Jackson, 2003).

PLATYPUS

Capture and Physical Restraint

Platypuses weigh 700 to 2400 g. Males possess a sharp spur on each hindleg that is connected to a venom gland located in the upper thigh region. Spurring and envenomation, although not fatal, are extremely painful (Jackson, 2003). Platypuses are more aggressive and their venom more potent during the breeding season (August to October). Consequently, extra care is required when handling them during this time.

Platypuses are usually restrained by holding them by the tail base (Figure 25.2). This keeps the spurs out of reach. Docile or hand-raised platypus can be cradled in the hands. Platypuses are easily transported in bags such as pillow cases.

Anesthesia

Platypuses are anesthetized using a mask placed over the bill and induced with isoflurane and oxygen. Platypuses are impossible to intubate because of their small gape, inability to visualize the larynx, and bulbous structure at the base of the tongue.

Vascular Access

A vascular sinus suitable for blood collection is located running transversely along the cranial border of the bill



Figure 25.1. A dorsally recumbent, anesthetized echidna demonstrating the technique for blood collection from the jugular vein.

(Figure 25.3). A 25-gauge needle, attached to a 2- to 3-ml syringe, is inserted on either side of the midline. Alternatively, a heparinized winged infusion set can be used as the needle is less likely to come out of the sinus if the platypus moves. Gentle pressure on the syringe is required to avoid collapsing the vessel. Blood can also be collected with greater difficulty from the ventral coccygeal vessels.



Figure 25.2. A manually restrained adult platypus demonstrating the correct position of the hand at the base of the tail to avoid the spurs in adult males.



Figure 25.3. Venipuncture can be achieved in platypuses by introducing a small gauge needle into the sinus at the edge of the bill.

Physiology

Normal body temperature is 32.5°C to 34.5°C, heart rate is 60 to 150 beats per minute, and respiratory rate is approximately 25 breaths per minute (Jackson, 2003).

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26 Marsupials Peter Holz

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INTRODUCTION

Marsupials are a diverse group of mammals comprising approximately 260 species located predominantly in Australasia, with representatives in North and South America (Tyndale-Biscoe, 2005). The subclass Marsupialia is divided into six orders: Dasyuromorphia (carnivorous marsupials), Peramelemorphia (bandicoots and bilby, *Macrotis lagotis*), Diprotodontia (koala, *Phascolarctos cinereus*), wombats (possums and macropods), Notoryctemorphia (marsupial mole, *Notoryctes typhlops*), Didelphimorphia (opossums), and Paucituberculata (shrew opossums).

ANATOMY AND PHYSIOLOGY

The physiology of marsupials is well described by Tyndale-Biscoe (2005). Marsupials have a lower metabolic rate than eutherians. However, they require higher dosages of injectable anesthetics than eutherians of similar size. For example, three times as much xylazine/ketamine is required to immobilize a possum than a cat of similar size. The reasons are unknown.

Marsupials have a lower body temperature than eutherians. Instead of a separate anus and urogenital opening they combine the two into a single cloaca. To effectively measure a marsupial's temperature the thermometer is inserted in the dorsal part of the cloaca, leading to the rectum. Thermoregulatory ability is slow to develop. For example, kowaris (*Dasyuroides byrnii*) cannot thermoregulate until about 100 days after birth. Consequently, it is important to provide supplemental heat if young animals, particularly unfurred, are anesthetised. Marsupials combat cold by shivering. They do not have brown adipose tissue, which is used by some eutherians to generate heat. They cope with excessive heat by panting and licking. Kangaroos, in particular, will lick their forelegs to keep cool.

The majority of marsupials weigh less than or equal to 10 kg (Table 26.1) and can be manually restrained

with minimal risk to the handler. Consequently, where possible, mask induction with isoflurane is the anesthetic technique of choice. Standard analysics and anti-inflammatory agents have been used at small animal dosages with no adverse effects. Venipuncture sites are listed in Table 26.2. Reference ranges for heart rate, respiratory rate, and body temperature for a variety of marsupials are given in Table 26.3.

DASYUROMORPHIA

Physical Restraint

Physical restraint is only used for either minor procedures or to induce general anesthesia, as it will lead to considerable struggling and attempts to bite. This will result in a minor degree of pain and inconvenience when caused by an antechinus or dunnart, but the larger members of the group (i.e., Tasmanian devil, *Sarcophilus* harrisii) will inflict severe injuries (Figure 26.1).

When restraining and transporting dasyurids, it is advantageous to place them in a bag. This can range from a pillowcase for the smaller animals up to a large hessian (burlap) sack for Tasmanian devils. Animals in bags tend to relax as outside stimuli and visual threats are removed. The chance of injury is also decreased since they cannot lash out against solid objects. It also disorients them, giving the operator the upper hand.

Small dasyurids are gripped by the scruff of the neck or held around the body and placed in a bag (Figure 26.2). Larger dasyurids (i.e., quolls and devils) can be caught in a net or restrained by the tail and then lowered into a bag. They should not be carried long distances held only by the tail. Devils must be closely monitored while in the bag as they can chew their way out. Smaller dasyurids (e.g., antechinus, dunnarts, and phascogales) should not be restrained by the tail as severe degloving injuries and tail fractures can occur. If quolls are held by the tail care is required as some are agile enough to turn and bite the handler. Most wild

Table 26.1. Body weights of selected marsupial species.

Species	Body Weight	Species	Body Weight
Tasmanian devil	7–9 kg	Ring-tailed	700-1,100 g
F (11	700 2 000	possum	750 1 700
Eastern quoll	700–2,000 g	Greater glider	750–1,700 g
Tiger quoll	1.5–5 kg	Feathertail glider	10-14 g
Brown antechinus	20-70 g	Sugar glider	95-160 g
Fat-tailed dunnart	10-20 g	Eastern grey kangaroo	3-66 kg
Kowari	70-140 g	Red kangaroo	17-85 kg
Brush–tailed phascogale	100-300 g	Red–necked wallaby	11-27
Southern brown bandicoot	400–1,600 g	Swamp wallaby	10-20 kg
Bilby	800–2,500 g	Tasmanian pademelon	2-12 kg
Koala	4-11 kg	Parma wallaby	3-6 kg
Common wombat	22-39 kg	Tammar wallaby	4–10 kg
Southern hairy-nosed wombat	19-32 kg	Marsupial mole	40-70 g
Brush-tailed possum	1.2-4.5 kg	Virginia opossum	2-5.5 kg

Table 26.2. Accessible veins in marsupials.

Ventral coccygeal vein (artery)

Insert the needle perpendicular to the tail in the ventral midline, and advance it until the vertebrae are reached. Withdraw the needle slightly and blood should enter the needle hub. This vein is useful for smaller dasyurids, possums and gliders, and macropods.

Femoral vein and artery

Direct the needle at the pulse felt in the inguinal region. Arterial blood is often obtained and digital pressure is required to prevent hematoma formation. This vein is useful for dasyurids, bandicoots, bilbies, koalas, wombats, possums, gliders, and opossums.

Medial metatarsal (saphenous) vein

This is a small vein running along the medial aspect of the hind leg. This vein is useful for small dasyurids, wombats, possums and gliders, and macropods.

Cephalic vein

This vein is present on the dorsal surface of either foreleg. It is useful for Tasmanian devils, quolls, bandicoots, bilbies, koalas, wombats, larger possums and gliders, macropods, and opossums.

Jugular vein

This vein is useful for dasyurids, bandicoots, bilbies, koalas, wombats, possums, gliders, and macropods, but can be difficult to access in wombats and possums because of their short necks.

Lateral coccygeal vein

A large vein is present on both lateral aspects of the tail. Applying pressure or a tourniquet to the tail base will raise the vein. This vein is useful for macropods and opossums.

dasyurids are small enough to be caught in Elliott traps baited with meat or pit fall traps.

Anesthesia

During induction it is important to grasp quolls and devils very firmly behind the head, as they will attempt to pull back out of the mask to bite the handler. Tasmanian devils and quolls have a wide gape and are easily intubated for more prolonged procedures (Figure 26.1).

If the animal cannot be masked induced, an injectable induction is required. Dosages are given in Table 26.4. Relaxation is variable with tiletamine/zolazepam

(TZ) and constant limb movement can occur in Tasmanian devils. Recoveries can also be prolonged, in excess of six hrs in one Tasmanian devil (Holz, 1992).

PERAMELEMORPHIA

Physical Restraint

Bandicoots and bilbies are nervous animals. Care is required with physical restraint as they will attempt to kick and can struggle so vigorously that spinal damage results. They have sharp teeth and will bite if provoked. To restrain a bandicoot grasp it firmly behind the neck between the first two fingers of one hand and support

Table 26.3. Heart rate, respiratory rate, and body temperature of selected marsupials.

Species	Heart Rate/Minute	Respiratory Rate/Minute	Temperature (°C)
Tasmanian devil	85-120	20	31-38
Bandicoot ^a		31-37	33-34
Sugar glider	200-300	16-40	35-36
Koala	65-90	10-15	35.5-36.5
Common wombat	90-120	20	35.4-36.7
Macropoda	60-150	10-30	35-36.5
Virginia opossum	90-160	12-24	35-36

^aHeart rate and respiratory rate varies with the species, the rate decreases with increasing body size.



Figure 26.1. A Tasmanian devil (Sarcophilus harrisii) demonstrating its large gape and powerful jaws.

the rump with the palm of the other. This form of restraint should only be used for minor procedures or to transfer the bandicoot into a bag. Bilbies can be grasped by the base of the tail and then transferred to a bag.

Anesthesia

Both bandicoots and bilbies can be mask induced and maintained on isoflurane and oxygen. Because of their wide oral gape, visualization of the glottis and intubation with a 2- to 3-mm endotracheal tube is not difficult.

KOALAS (DIPROTODONTIA)

Physical Restraint

Depending on the temperament of the koala manual restraint may be sufficient for blood sampling, examination, or minor treatments (Figure 26.3). However, care is



Figure 26.2. Physical restraint of an eastern quoll (Dasyurus viverrinus), a small carnivorous marsupial.

Table 26.4. Dosages (mg/kg) of tiletamine/zolazepam (TZ), xylazine/ketamine (X/K), and medetomidine/ketamine (M/K) for immobilization of marsupials.

Species	TZ	X/K	M/K
Dasyurids	10	4/20	
Bandicoots and Bilbies		10/30	
Koalas	4-10	5/15	
Wombats	3-8	4/20	
Possums and Gliders	10	6/30	
Macropods	10	5/10-25	$0.1/2^{a}$
Opossums	15	10/20	0.1/10

^aSee macropod section.

required when restraining agitated koalas that can deliver serious bites and painful scratches.

A koala high up in a tree will need to be anesthetized by dart. A combination of tiletamine/zolazepam (3.5 mg/kg IM) and medetomidine (55 μg/kg IM), reversed with atipamezole (2 mg IV), has been used successfully (Lynch and Martin, 2003). However, if it is within reach, the koala is coaxed down using a pole with a hessian (burlap) sack or piece of material tied to the end. Waving the sack just above the koala's head will encourage it to descend. When it is close enough a bag is placed over the koala's head, back, and finally over its rump. With the koala's body contained within the sack the claws are disengaged from the tree and the koala should tumble into the bag. It is important to keep the bag over the koala's head and detach the animal from the top down. Otherwise it will attempt to climb back up the tree (Jackson, 2003). One person can catch docile koalas. However, agitated animals need at least two



Figure 26.3. Physical restraint of a juvenile koala (Phascolarctos cinereus) adapted to human contact. These animals are still capable of injuring with their claws an unwary handler.



Figure 26.4. Blood collection from the cephalic vein of an awake koala restrained in a large bag.

people, one to cover the koala with the sack and one to detach its claws.

Once in the bag a foreleg can be extended for blood sampling from the cephalic vein (Figure 26.4). Detailed examination and treatment should be performed under general anesthesia. The koala can be safely transported in the bag. It is important to hold the bag away from the body and not sling it over the shoulder as the koala can bite and scratch through the bag.

Young hand-raised koalas can be carried on the handler's body, like a human child, with one hand supporting the rump (Figure 26.3). Make sure there is enough padding between the koala and the handler's skin, as claws will readily penetrate a shirt. Quiet adult koalas can be held with one hand on the scruff and the other supporting the rump.

Anesthesia

For mask induction the koala should be forced down onto the table using the handler's body weight. Koalas are very strong and the head must be firmly grasped as it is placed into the mask.

For prolonged procedures koalas should be intubated. Intubation is difficult as they have a narrow oral cavity and small gape. However, if the neck is extended and a long straight bladed laryngoscope is used it is possible to visualize the larynx. An endotracheal tube of approximately 3 to 5 mm internal diameter can then be passed.

If the koala cannot be restrained to induce inhalation anesthesia it will require an injectable induction (Table 26.4). Relaxation with tiletamine/zolazepam is variable and salivation may be excessive (Bush et al., 1990). This can be controlled with atropine (0.04 mg/kg IM, SC). Recoveries will take 3 to 4 hours. For short procedures propofol can be administered (6 to 8 mg/kg IV) (Vogelnest, 1999).

WOMBATS (DIPROTODONTIA)

Physical Restraint

Wild wombats are extremely strong and are very aggressive, inflicting painful bites on unwary handlers. Manual restraint should not be attempted. Hand-raised wombats may permit themselves to be carried. One or both arms should be placed under the axilla, behind the forelegs, and the wombat picked up. A hand may be used to support the rump (Jackson, 2003).

Anesthesia

A wild adult wombat is unlikely to allow mask induction and an injectable agent will be required (Table 26.4). Despite their bulk and short legs they can run as fast as a human and, given the opportunity, will rapidly dive down their burrow. As they are nocturnal chasing wombats can be extremely hazardous due to the danger of tumbling down an unseen burrow. To catch a wild wombat, blind it by shining car headlights or another powerful light at it. The handler should then approach the wombat in the dark, trap it with a net and inject it. Tiletamine/zolazepam is the combination of choice as it results in rapid induction and a good level of relaxation. For prolonged procedures wombats should be intubated. Intubation is difficult as they have a narrow oral cavity and small gape. However, if the neck is extended

and a long straight bladed laryngoscope is used it is possible to visualize the larynx (Booth, 1999).

POSSUMS AND GLIDERS (DIPROTODONTIA)

Physical Restraint

Many possums can scratch and the larger ones will deliver painful bites. They are often presented in boxes or other containers such as wire possum traps that make restraint difficult. A towel should be used to disorient them. Thick gloves can be worn but large possums are able to bite through these and they markedly decrease sensitivity. Once under the towel the possum is grasped firmly behind the head. Brushtail possums (Trichosurus spp.), in particular, are stronger than they appear and will pull back out of a grasp that is too lax. The handler is more likely to be bitten than strangle the possum, so be firm. It is also necessary to grasp the base of the tail with the other hand. Otherwise the possum will swing its hindlegs forward in an attempt to scratch. If the possum is then stretched out it can be examined or anesthetized. Alternatively, it can be placed firmly on a table, giving it purchase for its claws, decreasing the likelihood of being scratched. An inhalation anesthetic induction chamber may also facilitate restraint.

It is preferable to transport the animal in a bag or pillowcase. The animal's head can be grasped through the pillowcase, the material rolled back and the face placed in an anaesthetic mask for induction.

Anesthesia

If the animal cannot be restrained to induce inhalant anesthesia it will require an injectable induction (Table 26.4). Relaxation with tiletamine/zolazepam is variable and deaths occurred in three squirrel gliders (*Petaurus norfolcensis*) (Holz, 1992).

MACROPODS (DIPROTODONTIA)

Physical Restraint

Manual restraint is only used for minor procedures or prior to the induction of general anaesthesia. Macropods will attempt to kick the individual attempting to restrain them. Because of the size of the claw on digit four and the powerful hindlimb muscles this can result in serious injury to the handler. Macropods will also bite and can inflict painful injuries with their teeth. Large kangaroos should never be manually restrained, as their hindlegs cannot be adequately controlled. Chemical restraint is strongly recommended.

Smaller macropods can be caught in a net. Care is required with exhibit design (Jackson, 2003), since macropods will tend to run close to the fence when pursued. All poles and supporting structures must be outside the pen. The inside wall of the pen must be smooth with no protuberances. Patience and quiet are required.

Many species panic easily and may collide with the fence resulting in soft tissue trauma and cervical fractures.

Once caught in a net the macropod can be grasped by the base of the tail and lowered into a Hessian (Burlap) sack or pillowcase, depending on the size of the animal. It is important not to hold the bag against the handler's body while the animal is being transported. They can still kick or bite through the bag injuring the handler.

If restraint and examination of the conscious macropod is required small wallabies can be grasped by the tail base and held firmly behind the head. A second handler is required to restrain the hindlegs, which should be held above the hock. Otherwise, if the animal kicks out, it may break a leg. If the legs are held with one hand, place a digit between the legs to prevent injury. The animal can then be examined.

It is important to emphasize that animals restrained in this way, unless they are tame or hand-raised, will be extremely stressed and struggle vigorously against the restraint. It should only be used for short-term procedures or as a prelude to chemical restraint.

Anesthesia

Sedation suitable for transport will occur 5 to 20 minutes after diazepam injection (1–2 mg/kg IM). Duration of effect is approximately 1 to 2 hours. Azaperone (2 mg/kg IM) may also be used. Effects appear after 15 to 20 minutes and last for 3 to 8 hours.

For animals in bags anesthesia is induced by extracting the macropod's head and placing the face in the mask. In this way the handler is protected to some extent from the powerful hindlimbs as they are contained within the bag.

If the animal cannot be restrained to induce inhalation anesthesia it will require an injectable induction (Table 26.4). Tiletamine/zolazepam inductions are swift and the low volume required makes it an ideal combination for immobilization by dart. However, recoveries can be prolonged (1 to 5 hours). Ketamine combined with medetomidine provides superior relaxation to tiletamine/zolazepam and, if concentrated medetomidine (10 or 20 mg/ml) is used, is also suitable for remote immobilizations. It is, however, extremely expensive. Induction times are longer than with tiletamine/zolazepam (up to 20 minutes). It is important not to stimulate the animal during induction, as this will extend the time to recumbency or result in inadequate immobilization.

The author has successfully used a combination of ketamine (5 mg/kg IM) and medetomidine (50 μg/kg) for immobilization of docile red (*Macropus rufus*) and western grey kangaroos (*M. fuliginosus*). There are several published dosages for ketamine/medetomidine combinations in macropods (2–3 mg/kg/50–100 μg/kg, Shima, 1999; 2–3 mg/kg/40–80 μg/kg, Vogelnest, 1999; and 4 mg/kg/40 μg/kg, Pye and Booth, 1998). However, in

the author's experience these dosages are too low to induce effective immobilization in the more nervous eastern grey kangaroos. Relaxation in this species was improved using a combination of ketamine (5 mg/kg) and medetomidine (125 μ g/kg), but results were too erratic to recommend this regimen. This dosage also proved inadequate to restrain smaller macropods such as pademelons (*Thylogale* spp.) and Parma wallabies (*Macropus parma*). The addition of midazolam (0.1 mg/kg) may improve induction and relaxation but also prolongs recovery. For wild macropods the tiletamine/zolazepam combination is preferred.

Ketamine/medetomidine immobilization is reversed using atipamezole (IM or SC) at five times the dose of medetomidine. The author has successfully used this dosage IV with no adverse effects. Animals are standing, but still ataxic, approximately 10 to 20 minutes after reversal.

For prolonged procedures macropods should be intubated as they may regurgitate. Intubation is difficult as they have a narrow oral cavity and small gape. However, if the neck is extended and a long straight bladed laryngoscope is used it is possible to visualize the larynx. An endotracheal tube can then be passed. Generally the larynx is smaller than would be expected for an animal of that size. Alternatively the animal can be placed in dorsal recumbency and a guide catheter used to facilitate passage of the tube. Lidocaine sprayed on the glottis may assist passage of the tube.

Long-acting Tranquilizers

Many macropod species are naturally nervous and may benefit from the use of long-acting tranquilizers when settling into new exhibits. The author has successfully used a combination of zuclopenthixol decanoate (10 mg/kg IM) and pipothiazine palmitate (10 mg/kg IM) administered to red-necked wallabies (Macropus rufogriseus). This dosage is much higher than that recommended for hoofstock but lower dosages proved ineffective. Duration of effect was approximately 10 days (Holz and Barnett, 1996). Fluphenazine decanoate (2.5 mg/kg IM) has also been recommended (Vogelnest, 1999). Duration of effect was approximately seven days. In the author's experience fluphenazine produced no appreciable effect at this dosage when used in red kangaroos and eastern grey kangaroos. Higher dosages may be required.

NOTORYCTEMORPHIA

Marsupial moles are rarely found in captivity. They can be held in the hand and do not attempt to bite, but resent physical restraint (Jackson, 2003). They can

be mask induced and maintained with isoflurane anesthesia.

DIDELPHIMORPHIA AND PAUCITUBERCULATA

Physical Restraint

Opossums will defend themselves by biting, but they may also feign death. It is important to remain vigilant if this happens as the opossum may suddenly become active and either bite or attempt to escape. To restrain the opossum a towel should be placed over the animal, which can then be firmly grasped behind the head. They can also be lifted by grasping the base of the tail. However, some animals may be able to lift themselves to bite and require additional restraint around the nape of the neck.

Anesthesia

The opossum is placed in a bag for transport or mask induced with isoflurane. A plastic induction chamber, connected to an isoflurane machine, can also be used. If inhalation anesthesia is not possible an injectable induction is required. Dosages are given in Table 26.4 (Stoskopf et al., 1999).

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27

Insectivores (Hedgehogs, Moles, and Tenrecs)

Darryl J. Heard

TAXONOMY AND BIOLOGY

The Order Insectivora has traditionally been used to unite several disparate mammalian groups (i.e., hedgehogs, moles, tenrecs, shrews, and solenodons) based on size and "primitive characters" (Nowak, 1999). Recent revisions based on molecular evidence has redistributed insectivores into several orders: Afrosoricida (tenrecs and golden moles, 51 species), Erinaceomorpha (hedgehogs, 24), and Soricomorpha (moles, shrews and solenodons, 428) (Wilson and Reeder, 2005). For this discussion, however, these animals are grouped together.

The most commonly encountered insectivores in clinical practice in Europe and North America are the West European (Erinaceus europaeus) and four-toed or white-bellied (Atelerix albiventris) hedgehogs, respectively. The biology, anatomy, and physiology of hedgehogs are well described by Reeve (1994). Their major anatomical characteristic is their spines. Each is erected by a muscle originating in the deeper layers (Reeve, 1994). When threatened and unable to flee, hedgehogs usually roll into a ball using several specialized muscles. All spiny hedgehogs appear able to hibernate during adverse conditions. Hibernation is associated with polycythemia and relative hypoglycemia (Reeve, 1994). The "normal" body temperature of non-hibernating European hedgehogs is 35 ± 2°C (Reeve, 1994). Heart rate is approximately 200 to 280 bpm, declining to less than or equal to 25 bpm during hibernation.

Moles and shrews are occasionally encountered as injured wildlife. Torpor occurs in shrews, some golden moles and tenrecs (Reeve, 1994). Shrews have some of the highest metabolic rates, oxygen consumption rates, water turnover, and heart and respiration rates of any mammal (Ishii et al., 2002; Ochocinska and Taylor, 2005).

PHYSICAL RESTRAINT

All insectivores can bite. In addition to the trauma that may be inflicted, shrews have salivary venom, blarina toxin (Kita et al., 2004).

Reeve (1994) describes several techniques for unrolling a hedgehog. Leather gloves are worn to protect from the spines. If you are right-handed, gently lift the hedgehog's hind end in your right palm. Use your left hand under its front, head turned away from you. Gently bounce it up and down in your hands. The hedgehog will extend its feet and unroll its snout. Without hurrying, keep bouncing it gently and allow the snout to poke between the thumb and index finger of the left hand. Place the thumb on the back of its neck using gentle, firm pressure. This prevents it from tucking its head back down. Gently gripping the rear underside of the animal with your right fingers put your right thumb in the small of its back and gently open out the animal by flexing it backward. Alternatively, the rolled up animal is held head down over a table. It then usually unrolls cautiously and tries to reach the surface. The back legs can then be grasped gently and the animal held by them. Alternatively, the animals are transferred directly to an inhalant anesthetic induction chamber.

PREANESTHETIC PREPARATION

Fasting is not recommended because most insectivores are very small, have high metabolic rates and small glucose reserves, and are prone to develop hypoglycemia (see Chapter 60).

PARENTERAL ANESTHESIA

Description of parenteral anesthesia in insectivores is scant; drugs and dosages are extrapolated from those used in rodents (see Chapter 60). Although inhalation (isoflurane, sevoflurane) is preferred, parenteral anesthesia may be indicated for remote field work. Xylazine (3 mg/kg SC), and ketamine alone (20–30 mg/kg IM) or in combination with midazolam (1–2 mg/kg IM) will cause a hedgehog to unroll and allow examination (Reeve, 1994). Buprenorphine (0.01–0.03 mg/kg SC q12 hour) has been used by this author for analgesia.

Injection Sites

For SC injections in hedgehogs forceps are used to grasp a small fold of the spiny skin over the rump. Injection is made into the connective tissue at the base of the pleat formed with the needle parallel to the animal's body (Reeve, 1994). A skin fold can also be raised by pulling upward on a spine. Alternatively, an injection is made in the flank while a gloved helper pins the animal on a table. Intramuscular injections are made in the large muscles of the thigh, not the back. This route is avoided in most other insectivores because of the potential to cause irritation and self-trauma. Intraperitoneal injection is as described for rodents. Intravenous injection is difficult or impossible in most. Potential sites include cephalic (over the forearm) and intraosseous injection into the femur, tibia, and possibly the humerus.

INHALATION ANESTHESIA

Inhalation anesthesia provides rapid induction and recovery. An induction chamber can be constructed from a plastic container with an attachment for administration of the inhalant and another for removal of waste gases. Alternatively, a mask is held over the nose or used to completely enclose a small insectivore (Figure 27.1). Animals caught in traps are either dropped into the induction chamber, or the trap enclosed in a plastic bag for anesthetic administration.

Most insectivores are too small for endotracheal intubation. A large adult white-bellied hedgehog may be intubated with a 2-mm uncuffed endotracheal tube.

MONITORING AND SUPPORTIVE CARE

Monitoring and supportive care are as for rodents (see Chapter 60). The high metabolic rate, oxygen requirement, and water turnover of many insectivores (especially shrews) make them very susceptible to hypothermia, hypoglycemia, hypoxemia, and dehydration. All effort should be made to minimize the duration of anesthesia. As described, vascular access is very difficult or impossible to attain. Intraosseous catheterization of the humerus, tibia, or femur is a possible alternative. Monitoring should include pulse oximeter, Doppler flow detection, or ECG.



Figure 27.1. Inhalation anesthesia is preferred for anesthesia in all insectivores. This white-bellied hedgehog (Atelerix albiventris) is being induced with isoflurane in oxygen administered into a commercial dog mask connected to a non-rebreathing system.

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28

Edentates (Xenartha)

Gary West, Tracy Carter, and Jim Shaw

INTRODUCTION

Edentata are immobilized to facilitate diagnostic procedures and treatment of medical conditions in zoological institutions (Ferrigno et al., 2003). These species have also been immobilized for a variety of captive and field research projects (Carter, 1983; Shaw, Machado-Neto, and Carter, 1987; Deem and Fiorello, 2002; Herrick, Campbell, and Swanson, 2002). Although several studies have been done describing immobilization of these species, very little scientific data exists on anesthesia and monitoring of this Order (Table 28.1).

PRE-ANESTHETIC PREPARATIONS

The Edentata encompass animals with a wide range of body sizes and unique anatomical features (Wallach and Boever, 1983; Divers, 1986; Gillespie, 2003). Body weights of edentates are often underestimated prior to immobilization (Deem and Fiorello, 2002). Edentates are often characterized as heterothermic or incompletely homeothermic with wide ranges in normal body temperatures. For instance, sloths have a normal body temperature range of 24°C to 40°C. Body temperatures in edentates may be influenced by ambient temperatures. Captures should be avoided during cold or inclement weather conditions (Deem and Fiorello, 2002). The capture of free-ranging edentates during cold weather may prolong their recovery and contribute to post-immobilization mortality. Fasting smaller species of edentates for 4 to 6 hours is appropriate, and large species (giant anteater, giant armadillo, and sloth) should be fasted for 12 to 24 hours.

Preparation for the capture of free-ranging giant armadillos is labor intensive. The location of an active giant armadillo burrow must be made before capture can be attempted (Carter and Encarnacao, 1983). Giant armadillos will create new burrows nightly, unless they are rearing young (Carter, 1983). Occupied burrows are located using domestic dogs, or by observation of recent

digging activity at a burrow entrance. Large traps constructed of reinforced metal are set at the entrance of occupied giant armadillo burrows. As the armadillos exit their burrows, they enter the trap. The armadillo is confined in the trap by closing a metal door. The metal door is often propped open with a small wooden stick and the armadillo bumps the stick and the door closes. Capture teams must wait near the trap site and immediately immobilize the animals after they are caught, because giant armadillos often destroy the traps and injure themselves if they are left in the traps for prolonged periods of time (Figure 28.1).

PHYSICAL RESTRAINT

Most armadillos can be manually restrained by grabbing the animal by the sides (Figure 28.2). Gloves are often used to avoid claw or biting injuries. Euphractus, the sixbanded armadillo, readily bite handlers. Wild giant armadillos are typically captured in traps as previously mentioned, and caution should be used with this species, as they are powerful and can inflict serious trauma to handlers before being fully immobilized. Sloths can be manually restrained with gloves or nets. Two-toed sloths can move very quickly when harassed, and bite. Restrained sloths are capable of using their powerful forelimbs for pulling themselves closer to a restrainer's hand and inflict serious bite injuries using their large, sharp, caniform incisors. Individual sloths can be restrained for examinations, blood collections, or induction of anesthesia by holding in dorsal recumbency with forelimbs extended laterally over a flat surface at a distance where the sloth can not reach and bite. A second handler can help restrict hind limb movements.

Lesser anteaters can be restrained with gloved hands, or held by the tail for injections. In one study, animals were restrained with their head and forelimbs in a bag while held by the tail for hand injections of immobilizing agents (Fournier-Chambrillion, Fournier, and Vie, 1997). Lesser anteaters have powerful claws that must be

Table 28.1. Normal adult body weights of select Edentate species.

Giant armadillo <i>Priodontes maximus</i> Six-banded armadillo <i>Euphractus sexcinctus</i>	18–33 kg 3–6.5 kg
Three–banded armadillo <i>Tolypeutes</i> spp. Long–nosed armadillo <i>Dasypus</i> spp Fairy armadillo <i>Chlamyphorus</i> spp	1–2.0 kg 3–10 kg 100 g
Giant Anteater <i>Mymecophaga tridactyla</i> Lesser Anteater <i>Tamandua</i> spp	18–39 kg 2–8 kg
Silky anteater <i>Cyclopes didactylus</i> Two-toed Sloth <i>Choloepus</i> spp Three-toed Sloth <i>Bradypus</i> spp	0.4-0.8 kg 4-9 kg 3-5 kg



Figure 28.1. Reinforced metal trap placed at the entry to a Giant Armadillo (*Priodontes maximus*) burrow.



Figure 28.2. Manual capture of a Six-banded Armadillo (Euphractus sexcintus).

avoided. Giant anteaters have very powerful front limbs, with prominent claws, and are difficult to restrain manually. Wild giant anteaters can be pinned to the ground with forked wooden sticks, and immobilizing drugs are then administered by hand (Shaw, Machado-Neto, and Carter, 1987) (Figure 28.3). Nets should not be used for anteater capture as their lips and mouths may be easily abraded (Wallach and Boever, 1983).



Figure 28.3. Free-ranging Giant Anteater (Myrmecophaga tridactyla) being restrained with wooden forked stick and hand injected with immobilization drugs.

INDUCTION

All edentates can be effectively immobilized with cyclohexamine (ketamine or tiletamine) drugs in combination with benzodiazepines or α_2 -agonists. Such combinations include ketamine-midazolam, tiletamine-zolazepam, ketamine-xylazine, or ketaminemedetomidine. In smaller species of edentates manual restraint and induction with inhalants is preferred. All armadillo species except the giant armadillo can be manually restrained for mask or chamber induction with inhalants. Isoflurane or sevoflurane are very effective induction agents in these species. However, anesthetic induction with inhalants can be prolonged because of breath holding of most edentates. Wild armadillos have been induced with isoflurane-soaked cotton balls (Deem and Fiorello, 2002). Caution must be used with this method of administration, as isoflurane can be vaporized to very high concentrations at normal atmospheric pressures (up to 33%), and inhalant overdose could occur easily.

A variety of injectable immobilizing agents has been used effectively in armadillo species, and may be used in field conditions. These include: tiletamine-zolazepam, ketamine-midazolam, ketamine, ketamine-xylazine, or ketamine-medetomidine. Ketamine-medetomidine appeared to be a superior option in field conditions, because of the ability to reverse the medetomidine component (Fournier-Chambrillion, Fournier, and Vie, 1997). Tiletamine-zolazepam causes good muscle relaxation, but prolonged recoveries are a problem in freeranging species. Intraperitoneal or intravenous pentobarbital has also been used experimentally in armadillos, but does not have the margin of safety of other immobilizing combinations. Droperidol and fentanyl (Innovar-vet) in combination have also been used effectively in armadillos, but this combination is no longer commercially available in the United States (Thurmon, Tranquili, and Benson, 1996). Giant



Figure 28.4. Immobilized Giant Armadillo (Priodontes maximus) having ear tag applied.

Table 28.2. Doses for anesthetic induction agents in Edentata.

2-8 m/kg IM

5-10 mg/kg(k) + 0.2 mg/kg(Mi)

0.5-1.5 mg/kg(x) IM

2-4 mg/kg(k) + 0.02-0.04(M)

5-10 mg/kg(K) +

Armadillos Tiletamine/zolazepam

Ketamine + Midazolam

Ketamine + Medetomidine

Ketamine + Xylazine

Ketamine + Midazolam Ketamine Ketamine + xylazine	5 mg/kg(K) + 0.2 mg/kg(Mi) IM 10-15 mg/kg IM 5 mg/kg(K) + 1 mg/kg(X) IM
Ketamine + Medetomidine Sloths	5 m/kg(K)+ 0.02-0.07 mg/kg(M) IM
Ketamine + Medetomidine	3 mg/kg(k) + 0.02 mg/kg(M)
Tiletamine/zolazepam	2-6 mg/kg IM
Ketamine + Midazolam	5-10 mg/kg(K) + 0.2 mg/kg(Mi) IM
Anteaters	

armadillos are most easily caught in burrow traps, and are successfully immobilized with ketamine and xylazine given intramuscularly (Figure 28.4). Drugs should be administered with 16- or 18-gauge, 1.5-in. needles. Giant armadillos immobilized with ketaminexylazine are not routinely given α antagonists, but the use of the α_2 -antagonist, atipamezole at 0.1 mg/kg IM may help shorten recoveries (Table 28.2).

Sloth species can often be approached and hand injected for immobilization while they are perching or resting. As the drugs take effect, the sloth can be supported with gloved hands to avoid biting injuries. A sedated sloth that is incapable of holding onto a support branch but capable of biting can be manipulated into a restraint box or container until maximum effect of induction drugs is reached. Sloths may be manually restrained also, and induced by facemask using an anesthetic inhalant such as sevoflurane. However, sloths may hold their breath for prolonged periods, making mask inductions difficult. A variety of injectable immobilizing drug combinations have been used in sloths (Vogel, Thoisy, and Vie, 1998; Gilmore, Da-Costa, and Duarte, 2000). Ketamine-medetomine IM was found to be the best for field conditions because of its reversibility (Vogel, Thoisy, and Vie, 1998). Tiletamine-zolazepam IM is a safe and effective immobilizing drug in captive situations, but recoveries are prolonged. A combination of ketamine-midazolam is also a good choice for induction. Animals may need to be confined during recovery before allowing them to climb again.

Anteater species have been immobilized with a ketamine-xylazine (Shaw, Machado-Neto, and Carter, 1987) combination. Xylazine does not seem to cause regurgitation as reported in other species (Fournier-Chambrillion, Fournier, and Vie, 1997). In one study of lesser anteaters, increased ketamine doses seemed to increase relaxation, but also caused severe bradycardia (Fournier-Chambrillion et al., 2000). Giant anteaters can be induced with ketamine and α_2 -agonist combinations with good recovery after reversal of the α -agonist. Ketamine-medetomidine adequately immobilizes captive anteaters. In captive situations, blow darts can be used to administer immobilizing drugs. Giant anteaters can be darted in leg musculature. However, in freeranging giant anteaters, darting episodes caused severe agitation, longer induction, and incomplete immobilization. The preferred field capture method is to approach the animal from a downwind location, restrain it with a forked stick, and quickly administer the immobilizing agent by hand injection in a hind limb (Figure 28.3). Etorphine, in combination with diazepam and atropine, may be an effective immobilizing combination for giant anteaters (Gillespie, 1985; Gillespie and Adams, 2003). No cardiac or respiratory depression was noted, but details were not given on how these parameters were monitored (Gillespie, 1985; Gillespie and Adams, 2003). The advantage of the combination is rapid recovery after opioid antagonist administration. Salivation may be controlled by anticholinergics, but blood pressure monitoring is essential if anticholinergics are given in conjunction with α -agonists (Wallach and Boever, 1983; Sinclair, 2003).

MAINTENANCE

After immobilization, edentates are typically maintained in lateral recumbency. In a captive situation, anesthesia is maintained with inhalants, and the α -agonist drugs can be antagonized. α -Agonists are antagonized because they cause severe bradycardia,

bradyarrhythmias, decreased myocardial contractility, and likely cause decreased cardiac output. (Sinclair, 2003). Armadillo and sloth species are easily intubated with the aid of a laryngoscope, whereas anteater species are not routinely intubated. Anteaters have very small mouths, and appropriate-sized endotracheal tubes cannot be advanced orally (Gillespie, 1985; Gillespie and Adams, 2003). Giant anteaters may accommodate a 10- to 14-mm endotracheal tube, and tracheotomy supplies should be available for emergency situations. Armadillos can hold their breath and seem to tolerate hypoxemia better than other mammalian species (Thurmon, Tranquili, and Benson, 1996).

Often the front claws of giant anteaters are bandaged during anesthesia to prevent claw injuries to handlers. However, if the animal is adequately immobilized and monitored, this should not be necessary. In the field, immobilized edentates have their eyes covered with a blindfold to protect them from direct sunlight.

SUPPORT

Blood pressure can be monitored in edentates with indirect methods, since intravenous and intra-arterial access sites are challenging to locate in edentates. Catheterization may require a venous cutdown procedure (Gillespie, 1985; Gillespie and Adams, 2003). Intravenous access sites include the femoral and cephalic veins in all edentates. Sloths also have cubital veins and vertebral veins that can be used for blood collection (Divers, 1986; Wallace and Oppenheim, 1996). Anteaters and armadillos also have jugular or ventral tail veins. Jugular cutdown procedures have been used to administer intravenous fluids in giant anteaters, although thick skin and large salivary glands make this a challenging task (Gillespie, 1985; Gillespie and Adams, 2003). Cardiocentesis has been advocated for armadillos or sloths, but could have severe complications and cannot be recommended (Divers, 1986). Intraosseous or intraperitoneal fluid administration may also be appropriate in emergency situations.

It has been reported that armadillos will spontaneously recover from ventricular fibrillation with no treatment (Thurmon, Tranquili, and Benson, 1996). Armadillos can also tolerate longer periods of apnea and hypoxemia than most mammals (Thurmon, Tranquili, and Benson, 1996). Heart rates for immobilized armadillos range from 120 to 220 beats per minute and respiratory rates from 60 to 80 breaths per minute. Body temperatures in armadillos may range from 30°C to 35°C. Cardiac output studies have been done in three-toed sloths using a dye solution technique and this data was similar to domestic species (Gilmore, Da-Costa, and Duarte, 2000). EKG evaluation in the three-toed sloth has been completed (Silva, Duarte, and da Costa, 2005). Sloths have extreme lability in their blood pressure and

stress can have a great influence on these values (Gilmore, Da-Costa, and Duarte, 2000). Pulse oximetry has been used in the sloth and may be influenced by hypothermia, hypotension, and pigmentation of tissues. Sloths immobilized with ketamine/ α_2 -agonists or tiletamine/zolazepam exhibited hypoxemia based on pulse oximetry readings (Vogel, Thoisy, and Vie, 1998). However, blood gas values were not collected in these sloths to confirm these readings (Vogel, Thoisy, and Vie, 1998). The normal HR for sloths is 45 to 60 bpm, and RR 10 to 80. Anteaters may have HR of 110 to 160 bpm and RR of 10 to 30 bpm normally.

Capnography can be used in edentates and the readings are more accurate in intubated animals. The difficulty in locating arteries can make blood gas analysis challenging, but blood gases should be monitored when possible.

RECOVERY AND COMPLICATIONS

Severe cardiovascular abnormalities can occur when α -adrenergic agonist agents are used for immobilization (Sinclair, 2003). α -Adrenergic drugs can be antagonized with atipamezole, both as a treatment for negative cardiovascular effects and to hasten recoveries. Antagonism of benzodiazepines with the use of flumazenil may reduce recovery times. However, the short duration of flumazenil antagonism (60 minutes) makes its use impractical, since the duration of benzodiazepine effects can be up to 4 hours. Captured, free-ranging animals may require treatment of dart or injection sites to prevent screw worm infestation (Deem and Fiorello, 2002). Post-recovery excitement and self-trauma can occur if the animals are confined after recovery. Animals may pace excessively and injure claws and feet by pawing at shift doors.

Isoflurane administered by cotton balls was associated with post-capture mortality in armadillos (Deem and Fiorello, 2002). The authors suggest that liver failure may have been caused by isoflurane, although when properly administered, isoflurane is the least likely inhalant to cause liver damage (Steffey, 1996). In addition, anesthetic-induced hepatic damage would not cause liver failure for several days after anesthetic administration. The administration of isoflurane by cotton ball may have caused severe anesthetic overdose and cardiovascular failure, with resulting liver congestion. Vaporization of isoflurane in room air could reach 33% concentrations and cause inhalant gas overdose.

Hypothermia in field situations is possible and difficult to treat in remote locations. Trauma from capture in traps can occur as animals may rub their face or head on the traps. Claw trauma can occur from animals trying to escape enclosures after being darted.

Intubation of anteaters would require tracheotomy and close monitoring as they heal. Handling wild nine-banded armadillos in the Southeastern United States could expose human handlers to *Mycobacterium leprae* or *Sporothrix schenkeii* (Kaplan, Broderson, and Pacific, 1982; Wenker et al., 1998; Truman, 2005).

Respiratory arrest was suspected in a giant anteater immobilized with ketamine and xylazine (Strom, 2003). The animal began to breathe after the administration of doxapram hydrochloride. Doxapram stimulates respiratory centers in the central nervous system and increases ventilation, but is not effective during respiratory arrest. It is likely that the immobilizing drugs caused transient apnea.

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29 Tubulidentata and Pholidota

Jennifer N. Langan

INTRODUCTION

Data on captive husbandry, medicine, and anesthesia of both aardvarks and pangolins in captivity are very limited. They are infrequently kept in zoos and are not favored as exhibit specimens because of their inactivity and nocturnal propensities. Some specimens of aardvarks have lived up to 20 years in zoological institutions, but the life span of captive pangolins has been significantly less.

TUBULIDENTATA

The aardvark (Orycteropus afer) is the only living representative of the order Tubulidentata. Their natural habitat is confined to Africa south of the Sahara Desert. They have solid bodies, a long snout, and powerful legs. They have long spadelike toenails that are used to dig burrows, find food, and defend themselves. Aardvarks range in weight from 50 to 70 kg. The animal's thick skin is covered with bristly hair. Aardvarks have a long extensible tongue used to collect termites and ants in the wild. Their teeth lack enamel and are continuously growing; this predisposes them to malocclusion and dental disease. Their cheek teeth are composed of numerous hexagonal prisms of dentin surrounding a tubular pulp cavity. This pattern of growth gives the order its name, Tubulidentata (tubule-toothed). The dental formula for aardvarks is I 0/0, C 0/0, P 2/2, M 3/3 (Figure 29.1). They are primarily nocturnal and sleep most of the day in underground burrows (Nowak, 1991).

Aardvarks can be conditioned to allow physical examination and minor clinical procedures (skin scrapes, conjunctival swabs) without chemical restraint but sedation is usually required for noxious or invasive procedures such as venipuncture. Aardvarks are extremely strong animals with an incredibly powerful kick. Manual restraint of adult aardvarks is not recommended. Neonates and juveniles can be physically restrained for procedures but should be sedated once

they are greater than 10 kg to prevent injury to the animal and the handler.

Chemical restraint for aardvarks is generally required for most medical procedures. A variety of anesthetic agents have been used successfully in aardvarks. A combination of ketamine and medetomidine intramuscularly, is currently one of the most widely used anesthetic protocols (Table 29.1) (Langan, 2003; Stetter, 2003). This combination provides rapid, smooth inductions, and at least 30 minutes of anesthesia. In the author's experience hand injection has not yielded consistent drug delivery because of the explosive reaction of the aardvark upon needle insertion. Contrastingly, remote drug delivery using CO₂ propelled darts has provided excellent results. However, owing to the aardvark's extremely tough skin, several modifications to dart removal have been needed. Pliers are used to pull out intramuscular darts and pressure is applied around the area of needle insertion to prevent subcutaneous air accumulation during dart withdrawal. When invasive or painful procedures are necessary supplementation with gas anesthesia is recommended. At the completion of the procedure atipamezole is given intramuscularly, to antagonize the effects of medetomidine and speed recovery. Recoveries are substantially smoother if the reversal is given at least 30 minutes after induction when medetomidine and ketamine are used in combination. Other successful drug combinations have included: tiletamine and zolazepam, ketamine, and detomidine (Vodicka, 2004), ketamine and xylazine (Nel et al., 2000), ketamine and midazolam (Nel et al., 2000), ketamine and droperidol in combination with fentanyl (Dieterich, 1986), and etorphine with acepromazine (Stetter, 2003) (Table 29.1).

Inhalant anesthetics reported in aardvarks include both halothane and isoflurane (Nel et al., 2000; Langan, 2003; Stetter, 2003). Animals can be maintained with gas anesthesia using either a mask or endotracheal intubation. Precautions should be taken to prevent nasal edema caused by tightly fitting face masks or gauze used to secure the endotracheal tube. Medical problems seen in aardvarks in captivity, such as conjunctivitis, post-operative wound dehiscence, and decubital ulcers can be treated by maintaining animals on a face mask using isoflurane.

Dental disease is by far the most common medical problem reported in captive aardvarks. Tooth root abscesses typically present as painful firm swellings. Buccostomies are often required to access teeth that need to be extracted because of the small size of the oral opening (Figures 29.2 and 29.3). Curettage to remove surrounding infected bone can lead to significant hemorrhage associated with dental infections. Endotracheal intubation in these cases is especially important to protect the animal's airway. The long and narrow oral cavity of the aardvark can make intubation challenging. Blind intubation with a size 10 mm endotracheal tube for adult aardvarks has been very reliable for the author. Following induction, the animal is placed in sternal or lateral recumbency and the animal's head and neck are maximally extended. Gentle traction is used to pull the tongue cranially out of the oral cavity (Figure 29.4), at which point the endotracheal tube is advanced over the base of the tongue. While holding one's ear to the proximal open end of the tube, the tip of the endotracheal tube is slowly moved into the larynx to the position at which maximal audible respiratory sounds and



Figure 29.1. Normal dentition of the aardvark. Dental formula I 0/0, C 0/0, P 2/2, M 3/3.

expiration are noted. Frequently the tube is inadvertently advanced past this point and introduced into the cranial esophagus instead of the trachea. This happens most frequently when the animal is still swallowing. Supplementing with isoflurane via a mask until the animal no longer swallows makes intubation much simpler. While ausculting and watching the chest cavity, the tube is gently advanced into the trachea during inspiration. Rotation of the tube during advancement facilitates placement of the endotracheal tube. Alternatively, a long slender-bladed laryngoscope or flexible endoscope may be helpful to facilitate intubation; but these typically are not necessary in the author's experience. The tongue should be manually returned to the oral cavity after the animal is intubated to prevent lingual edema. In one instance, an animal was unable to retract its edematous tongue and subsequently stepped on it, causing a severe laceration during recovery. The animal later required amputation of the distal third of its tongue. Because of the very small oral opening and depth of the cavity, dental examination with a laryngoscope blade prior to intubation is essential. Once the endotracheal tube is in place, there is insufficient space to do a thorough dental and oral examination.

It is the author's experience that many aardvarks pace excessively once they recover from anesthesia, causing excessive wear and bleeding of the toenails during the first 24 to 72 hours following immobilization. Oral diazepam given once a day at 10 mg/aardvark in the late afternoon has prevented excessive pacing behavior during their nocturnal activity.

Occasionally, females are extremely restless and do not allow their infants to nurse sufficiently or injure them inadvertently because of excessive activity in the nest box. In these cases, low doses of oral diazepam (0.25–0.45 mg/kg SID-BID) have alleviated this behavior and allowed successful rearing of the calf by the dam. The female is weaned off diazepam after 3 to 4 weeks, once the infant is sufficiently ambulatory and is more efficient at nursing.

Data from aardvarks that have been anesthetized between 1999 and 2006 at Brookfield Zoo have included heart rates ranging from 60 to 95 beats per minute, respiratory rates between 12 and 18 breaths per minute, and temperatures of 95°F to 100°F.

Table 29.1. Chemical restraint agents used for aardvarks.

Immobilization Drug	Dose	Antagonist	Dose	Reference
Tiletamine/zolazepam Ketamine/medetomidine	4–5 mg/kg 3 mg/kg and 0.03–0.07 mg/kg	Flumazenil Atipamezole	0.01 mg/kg 0.15-0.4 mg/kg	Langan Langan
Ketamine/detomidine Ketamine/midazolam	4–8 mg/kg and 0.09–0.18 mg/kg 15–20 mg/kg and 0.28–0.68 mg/kg	Atipamezole	0.05-0.09 mg/kg	Vodicka Nel
Ketamine/xylazine Ketamine/diazepam	14 mg/kg and 0.24 mg/kg 11 mg/kg and 0.26 mg/kg	Atipamezole	0.3 mg/kg	Nel Goldman



Figure 29.2. The narrow oral opening of the aardvark makes endotracheal intubation and oral examination more challenging.



Figure 29.3. The narrow oral opening of the aardvark makes endotracheal intubation and oral examination more challenging.



Figure 29.4. Withdrawing the aardvark's long tongue out of the mouth provides the needed space within the oral cavity and larynx to intubate the animal with an endotracheal tube.

Anesthetic monitoring using auscultation, pulse oximetry, ECG, and temperature is as in other mammals. Blood collection and intravenous catheterization can be best accomplished from the medial saphenous vein (Figure 29.5), but is also possible using the cephalic, ventral tail, or facial vein. Frequently, peripheral vessels appear to contract during venipuncture attempts, yielding very little blood despite large vessel diameter and good blood pressure. Large-bore (18-gauge) needles and slow manual syringe collection appear to yield the best results. The aardvark's skin is extremely thick and tough, often necessitating a modified cut-down procedure for catheter placement. The location of catheter placement is selected and appropriately prepared by clipping the fur and disinfecting the skin. The skin over the vessel is pulled lateral to the vein and a scalpel blade is used to make a small stab incision through the skin. The skin is then allowed to return to its normal position over the vessel, at which point the intravenous catheter can be routinely placed.

Infrequent monitoring of blood pressure has been attempted using a cuff distal hind limb and proximal tail with varying results. Arterial blood samples for blood gas analysis are easily obtained from the femoral or auricular artery. Arterial catheterization for continuous direct blood pressure monitoring would also likely be possible from the auricular artery. Field techniques used to capture free-ranging aardvarks include the use of nets and funnel traps set at burrow entrances. All



Figure 29.5. Venipuncture from the medial saphenous vein in an aardvark.

animals require immobilization to be handled and examined (Nel et al., 2000).

PHOLIDOTA

Animals belonging to the order pholidota include one genus (Manus) and seven species and are often referred to as scaly anteaters. The white-bellied tree pangolin (*M. tricuspis*), long-tailed tree pangolin (*M. tetradactyla*), giant pangolin (M. gigantean), and Cape pangolin (M. teminckii) are African, whereas Asia is inhabited by the Indian (M. crassicaudata), Chinese (M. pentadactyla), and Malayan pangolins (M. javanica). Some are arboreal and have strong prehensile tails, whereas others live in burrows. Pangolins attain a weight of 4 to 27 kg, with males being larger than females. They feed primarily on ants and termites at night, which they mechanically digest in a crop-like stomach modified for the grinding process (Wilson, 1994). Pangolins have stout powerful clawed limbs used for digging and long, ribbon-like tongues. The musculature of the tongue is remarkable and has attachments reaching along the xiphoid all the way to the pelvis. It retracts into a sheath in the chest cavity when at rest. Pangolins have very well-adapted salivary glands that extend posteriorly, nearly to the shoulder. The glands produce sticky secretions that facilitate the collection of their insect prey. Pangolins completely lack teeth, and the lower jaw is a small bladelike bone. The most obvious feature of pangolins is their scaly epidermal armor. The dorsal surface of their elongate body is covered in continuously growing, overlapping scales. Confronted with a threat, pangolins curl into a tight ball to protect their soft under parts and spray urine and noxious anal gland secretions (Nowak, 1991).

Large pangolins must be handled with caution because their surprising strength and sharp body coverings can injure personnel. Smaller specimens may be safely restrained with leather gloves. The normal pangolin behavior upon handling is to curl into a protective ball. Forced manual attempts to uncoil a pangolin can result in injury to the animals, and chemical restraint is typically advised to permit examination and specimen collection. Captive animals can be accustomed to handling and may become quite tractable, which facilitates routine veterinary procedures (Heath and Vanderlip, 1988; L. Greer, personal communication).

Historically, ketamine has been used for sedating *M. pentadactyla* (Heath, 1986) and *M. tetradacyla* (Robinson, 1983), with doses of approximately 16 to 25 mg/kg, administered IM in the hind limbs. Uncoiling is possible at the higher dose; however, some muscle tone persists and salivation occurs. The duration of effective restraint is relatively short (10–20 minutes)

(Robinson, 1983). More recently, chamber or mask induction and maintenance with isoflurane has replaced injectable anesthesia with excellent results (L. Greer, personal communication).

Resting heart rates have been reported to range from 80 to 86 beats per minute and respiratory rates varied from 14 to 53 breaths per minute (Heath and Vanderlip, 1988).

Literature on clinical medicine of pangolins is sparse. The most common reported disease concerns are related to gastrointestinal ailments. Captive pangolins have the propensity to ingest bedding materials (wood shavings, saw dust), which have resulted in gastric impactions and death (Griner, 1983; Heath and Vanderlip, 1988). Inappropriate diet, parasitism, and malnutrition are commonly reported problems in the literature (Kuehn, 1986; Heath and Vanderlip, 1988; Robinson, 2003). One source reports that pangolins appear to be highly susceptible to *Cryptococcus* spp. when they were housed in mixed species exhibits (Wilson, 1994).

Conventional peripheral vessels are difficult to access. Blood sampling can be accomplished under chemical restraint from a ventral surface of the tail by clipping a portion of a scale to gain access to the skin (Heath, 1986; Heath and Vanderlip, 1988).

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30

Chiropterans (Bats)

Darryl J. Heard

INTRODUCTION

After rodents, bats are the most diverse and widely distributed mammal group (Wilson and Reeder, 2005). They are also the most abundant and form the biggest mammalian aggregations known (Nowak, 1999). The order Chiroptera contains 18 recent families and greater than or equal to 1,116 bat species (Wilson and Reeder, 2005). It is divided into suborders Microchiroptera and Megachiroptera. The latter comprises just one family, the Pteropodidae, with 42 genera and greater than or equal to 186 species.

Bats inhabit most of the temperate and tropical areas of the world, except for some remote oceanic islands and beyond the tree growth line in the colder parts of either hemisphere. The Megachiroptera are confined to the tropical and subtropical regions of the Old World, east to Australia and the Caroline and Cook Islands.

PHYSIOLOGY AND ANATOMY

The word Chiroptera is derived from the Greek *cheir* (hand) and *pteron* (wing). Skeletal adaptations for flight include a keeled sternum and elongated second to fifth metacarpals that form long rigid spokes for wing membrane. The thumb (digit one) is an agile grasping tool, and the only digit with a functional claw. The thoracic vertebrae are interconnected to form a rigid column that supports the flight muscles.

Compared with other mammals, the acetabular opening is rotated and shifted dorsally, and the legs are rotated 180 degrees around their long axis so the knees face the rear. Since they usually perch inverted, their legs are adapted for pulling rather than pushing. At rest the entire body weight is suspended from the toes. Most have a locking mechanism that keeps the claws in a flexed position without muscular contraction. Consequently, bats must be "unhooked" from a perch rather than pulled; excessive force will injure toes and in juveniles cause epiphyseal fractures. The hind limb claws are compressed into

hooked blades that will lacerate skin during restraint of larger bats.

The maximal aerobic capacities are the same as similar sized birds. The minimal metabolic requirement in level flight is at least $1.5 \times$ greater than the maximal aerobic capacity of a similar sized nonflying mammal. Consequently, bats at rest are not likely to manifest overt clinical signs until respiratory dysfunction is well advanced.

Active bats are homeotherms, maintaining their body temperature between 35°C and 39°C. They use a large amount of energy to compensate for heat loss owing to a high body surface area to metabolically active tissue ratio. Additionally, large lungs and naked flight membranes result in heat loss from a surface area six times larger, and a thermal conductance 1.5 to 4 times greater than wingless animals. Some bats compensate for this with heterothermy; temperate bats and tropical Vespertilionids and Molossids have a variable ability to lower body temperature and go into torpor (diurnal lethargy) or hibernation. This is based not only on temperature, but also food availability and reproductive condition. Lowered body temperature and metabolic rate in hibernating or torpid animals is assumed to reduce anesthetic requirement, and alter drug uptake and elimination.

Bats consume large quantities of food relative to their body size. Gastrointestinal transit is also very rapid, possibly to minimize body weight for flight. Therefore, vomiting is unlikely unless animals are anesthetized immediately after feeding. Bats usually feed at night when they are most active. Consequently, blood glucose and tissue glycogen levels are lowest at dusk before the animals begin feeding (Widmaier and Kunz, 1993).

ZOONOTIC DISEASES

Bat populations are known reservoirs for several infectious agents of significance to humans and other animals (e.g., Lyssaviruses, Henipaviruses, *Leptospira* spp.)

(Constantine, 1970; Rupprecht, Stohr, and Meredith, 2001; Calisher et al., 2006). All personnel working with bats must be vaccinated against rabies and other lyssaviruses (Rupprecht, Stohr, and Meredith, 2001). Care is taken to minimize contact with blood, saliva, and other secretions or emissions that may contain infectious organisms. Although the teeth of many microchiropterans are very small, they can still penetrate human skin. Further, saliva contact with skin is also a possible source of infection. It is recommended that bats be anesthetized for procedures requiring close contact to reduce biting and transmission of secretions.

PHYSICAL RESTRAINT

Techniques used for capturing free-living bats are described by Kunz and Kurta (1988). All restrained bats are capable of delivering a defensive bite. Most have jaws that are shortened, giving them a powerful bite. Neonatal bats possess needle-like, caudally directed milk teeth for gripping the nipple. The thumbs and associated claws of large bats will scratch an unprotected handler and are used to pull fingers in for a bite.

Bats are restrained with leather gloves (Figure 30.1 A,B). Alternatively, a towel is used to cover the head and confine the limbs. In small bats nets can be used for initial capture, but are cumbersome in larger animals. However, they should always be available in case of an escape. The duration of manual restraint is minimized to reduce stress and prevent hyperthermia. Prolonged restraint induces marked elevations in cortisol and glucose (Widmaier and Kunz, 1993). Carrying cages must be sufficiently tall to prevent the head of the bat from touching the floor.

Wimsatt et al. (2006) describe the use of a restraint device made of polyvinyl chloride tubing in big brown bats (*Eptesicus fuscus*). An attachment at one end is used to administer inhalant anesthesia.

BLOOD COLLECTION AND HANDLING

The blood volume of active bats is approximately 9.0 to 11.0 ml/100 g. Blood is collected in bats greater than or equal to 100 g from the median artery or vein on the medial aspect of the distal humerus with a 25-g needle and 1- or 3-ml syringe (Figure 30.2). If the collector is right-handed, the right wing of the supine bat is extended until the elbow joint forms a 90-degree angle. The left hand of the collector is then used to rotate the biceps muscle laterally while compressing the median veins to cause their distention. The right hand is supported on the table surface and the needle and syringe rest across the proximal radius as the needle enters the vessel. Once blood is identified in the needle hub, continued flow must be "finessed" with gentle alteration in suction, rotation of the needle, and patience. There are





Figure 30.1. A. Leather gloves are recommended for handling even small bats, such as this evening bat, from bites. **B.** Physical restraint of a large flying fox (Pteropus vampyrus) for sample collection. Note the use of long-sleeved gloves to protect the holder from scratches, and the hold around the neck and feet.

usually two or more veins and an artery in close contact at the insertion site. Although arterial blood can be used for sampling, care must be taken to ensure adequate hemostasis. Large hematomas are common, even with venous puncture, and in small bats may result in death. Since collection time may be prolonged, heparinization of the syringe is recommended when a plasma sample is appropriate (Heard, Ruiz, and Harr, 2006). However, if collection lasts greater than 2 minutes and is traumatic, the anticoagulant effect of the heparin will be overcome by thromboplastin released from tissue. Further excessive pressures will result in hemolysis.



Figure 30.2. Venipuncture of the right median vein in an anesthetized large flying fox (Pteropus vampyrus). Note the positioning of the elbow in a right angle to facilitate access to the vessels on the ventral aspect of the distal humerus.

In small bats, blood samples are collected from the cephalic vein along the leading edge of the patagium (Figure 30.3). A 25-g needle is used to make a hole in the vessel and blood is collected into a microhematocrit tube from the incision site. Alternatively, a 0.5-ml insulin syringe with attached 27-g needle is used. This technique is also used to collect blood from the saphenous (interfemoral) (Figure 30.4) vessels. In very small bats the uropatagial vessels can be dilated with the application of a warm pack (Wimsatt et al., 2006).

The external jugular veins are large in microchiropterans and may in some species be used for collection. Cranial vena caval collection has also been successful in some large bat species. The internal and external jugular veins of Megachiropterans are small and of similar size.

Bat blood is easily altered by inappropriate collection, handling, and storage. Even moderate hemolysis during sample collection will cause pseudo-hyperkalemia, hyponatremia, hypochloremia, and elevated aspartate transaminases (Day, Heard, and Leblanc, 2001). Hyperkalemia in otherwise healthy animals is usually an indication of sample collection error. If the plasma remains in contact with the red cells for greater than or equal to 6 hours, there will be an elevation in phosphorus and decreases in chloride and glucose concentrations (Day, Heard, and Leblanc, 2001). Heparinized blood samples



Figure 30.3. Venipuncture of the cephalic vein in an anesthetized Egyptian fruit bat (Rousettus aegyptiacus).



Figure 30.4. The saphenous (interfemoral) vein in the uropatagium of a microchiropterans, a Mexican free-tail bat (Tadarida brasiliensis). This vessel can be used for small-volume blood collection.

allow centrifugation immediately after collection and the plasma to be removed from the blood cells and frozen until analysis (Day, Heard, and Leblanc, 2001; Heard, Ruiz, and Harr, 2006).

PARENTERAL ANESTHESIA

Inhalation anesthesia is preferred in bats. However, there are circumstances in which it is neither available

Table 30.1. Anesthetic and Analgesic Drugs Used in Megachiropteran and Microchiropteran Bats.

	Dosage				
Drug	Route	Megachiroptera	Microchiroptera	Comments	
Parenteral Ketamine	IM	40–50 mg/kg	≥100 mg/kg	Not recommended because of poor muscle relaxation, and prolonged recovery with wing flapping.	
Xylazine/ ketamine	IM	Combine equal volumes xylazine (20 mg/ml) and ketamine (100 mg/ml); 0.4 ml/kg		Variable flying fox (<i>Pteropus hypomelanus</i>) (Heard et al., 1996). Australian flying foxes (<i>Pteropus</i> spp.) (A. Olsson, personal communication)	
Medetomidine/ ketamine	IM	Combine equal volumes medetomidine (1 mg/ml) with ketamine (100 ml/kg); 0.5 ml/kg		Variable flying fox (Heard et al., 2006).	
Tiletamine/ Zolazepam	PO	40 mg/kg		For immobilization of large bats when physical restraint is dangerous (i.e., suspect rabid bats or animals caught in barbed wire). Drug combination is squirted into mouth of animal (Vogelnest, 1999). Recovery is prolonged; not recommended for routine anesthesia/immobilization.	
Propofol	IV	6–8 mg/kg	8–10 mg/kg	Dilute 1:4 with saline to obtain injection volume in small bats (A. Olsson, personal communication).	
Inhalation					
Halothane	Inhalation	Induction 4%–5%, maintenance 1%–1.5%			
Isoflurane	Inhalation	Induction 5%, maintenance 2.5%			
Sevoflurane	Inhalation	Induction 6%–7%, maintenance 3%–4%		Expensive	
Analgesics					
Butorphanol Buprenorphine	SC, IM SC, IM	0.4 mg/kg q 4 hr 0.03 mg/kg q 6–12 hr	2 mg/kg q 4 hr 0.05–0.1 mg/ kg q 6–12 hr		
Morphine Carprofen Meloxicam Tramadol	SC, IM SC, IM, PO SC, IM, PO PO	0.5–1.0 mg/kg q 4–6 hr 1–4 mg/kg q 24 hr (q 12 hr PO) 0.1–0.3 mg/kg q12 hr 0.5–2.0 mg/kg q24 hr	2–5 mg/kg q 4 hr 3–5 mg/kg q12 hr 1–2 mg/kg q12 hr		

nor appropriate to the situation (i.e., anesthesia of freeliving animals in remote locations). Parenteral anesthetic regimens are summarized in Table 30.1.

Injection Sites

When possible, intramuscular injection in the flight muscles is avoided. However, in large aggressive bats it is easier to press them into sternal recumbency and administer drugs in the large triceps or thigh muscles. The sternum is relatively narrow and pectoral muscle injection may result in the needle passing between the ribs if the bat moves.

Intravenous injection sites are the same as those used for blood collection: cephalic (Figure 30.5), median, and femoral or saphenous. Small-gauge catheters are placed temporarily in the cephalic and median veins. Awake

bats usually do not tolerate catheters. Intraosseous catheterization of the radius is an alternative route for administration of fluids. This route can be used in even the smallest bats.

Microchiropterans

Although there are several examples of "big" little bats, most Microchiropterans are less than 50 g. Small body size is usually associated with a higher anesthetic dosage required for a given level of analgesia or anesthesia. Most reported studies of parenteral anesthetics in Microchiropterans investigate their effects on wing membrane capillary function; no mention is made of anesthetic effect (Harris, Hodoval, and Longnecker, 1971; Longnecker and Harris, 1972; Longnecker, Miller, and Harris, 1974).



Figure 30.5. Cephalic vein catheterization in an anesthetized large flying fox (Pteropus vampyrus). Most bats are intolerant of catheters when awake. Care is taken to not compress the patagium (wing membrane) within constrictive bandages.

Megachiropterans

In variable flying foxes (*Pteropus hypomelanus*), ketamine alone (30–37.5 mg/kg IM) produced short-term chemical restraint, but poor muscle relaxation and struggling during recovery (Heard, Beale, and Owens, 1996).

In the same species, xylazine (2 mg/kg IM)/ketamine (10 mg/kg IM) and medetomidine: ketamine (50 µg/kg: 5 mg/kg IM) combinations produce short-term immobilization (30 minutes) with good muscle relaxation and quiet recovery (Heard, Beale, and Owens, 1996; Heard, Towle, and LeBlanc, 2006). During induction with medetomidine/ketamine the palpebral response was lost first, followed by clinch and bite response (Heard, Towle, and LeBlanc, 2006). These responses returned in the reverse order during recovery. It is recommended that xylazine or medetomidine not be reversed, except in an emergency, because the adverse effects of ketamine (wing flapping and struggling with associated hyperthermia) will be unmasked during recovery. In other bat species the dosages/kg are increased as the size of the animal decreases.

Tiletamine/zolazepam (20–40 mg/kg) produces immobilization, but prolonged recovery. However, it has been used to immobilize free-living animals suspected of being rabid or trapped in barbed wire (Vogelnest, 1999; A. Olssen, personal communication). The drug combination is sprayed into the open mouth, preventing contact with people until anesthetized.

Propofol (8–10 mg/kg IV) provides 5 to 15 minutes of anesthesia in animals in which a vessel can be accessed for injection. Propofol may be diluted 1:4 with saline to facilitate administration (A. Olsson, personal communication). Rapid injection is associated with marked cardiopulmonary depression and possibly apnea; endotracheal tubes, laryngoscope, and a mechanism for providing assisted ventilation must be available.

INHALATION ANESTHESIA

Inhalation anesthesia is very safe and effective in both captive and free-living bats (Wimsatt et al., 2006). An efficient respiratory system (Canals et al., 2005) makes induction and recovery times comparable to those of birds. Isoflurane (5% by mask, then maintenance 2%–2.5%) provides rapid (1–2 minutes) induction and recovery, as well as rapid response to changes in vaporizer setting. For prolonged anesthesia, bats are attached to a non-rebreathing system with either an endotracheal tube or mask (Figure 30.6). Portable, lightweight inhalant anesthetic systems developed for avian anesthesia are ideal for field immobilization (see Chapters 5, 22, and 23).

Endotracheal Intubation

Bats greater than or equal to 150 g are intubated with a greater than or equal to 2-mm internal diameter endotracheal tube. For intubation the author prefers to place the bat in dorsal recumbency to visualize the glottis (Figure 30.7). The mouth is opened using gauze placed around the upper and lower jaws and the tongue pulled forward and to the side. A laryngoscope with a small straight pediatric blade is used for illumination. Topical anesthetic applied to the glottal opening decreases reflex coughing. Glycopyrrolate (0.01 mg/kg IM) administered before induction will reduce the sometimes profuse pharyngeal secretions.

Monitoring

Cardiovascular Heart rates range from 100 beats per minute (bpm) in resting large Megachiropterans to almost 1,000 in the smallest. Heart rates are influenced by restraint, anesthesia, environmental temperature, and size. The rate of the 5 to 10 g Myotis lucifugus ranges from around 350 bpm at thermoneutrality (33°C-38°C) to as low as 6 bpm during hibernation (rectal 6°C) (Kallen, 1977). Although the electrocardiogram is typically mammalian, its configuration in Microchiropterans varies with rate and there are species differences. In some Vespertilionids at high rates the T and R waves fuse, and the P wave is difficult to identify. Active and dormant bats may develop a functional bradycardia interrupted by transitory compensatory tachycardias. At low body temperatures, supraventricular arrhythmias and second-degree heart block are common, but reverse with warming. However, bats appear resistant to hypothermia-associated ventricular fibrillation (Kallen, 1977). Heart rate and rhythm and peripheral blood flow are assessed with a Doppler flow probe secured over the tibial artery behind the knee or the pedal artery on the palmar surface of the feet.

Respiratory Hemoglobin saturation and heart rate are monitored with a pulse oximeter probe placed on the tongue, foot or median artery, or with a rectal reflectance



Figure 30.6. Medium to large bats, as in this Wahlberg's epauletted fruit bat (Epomorphorus wahlbergi), can be intubated with commercially available endotracheal tubes (greater than or equal to 2 mm ID). The trachea is relatively short and the endotracheal tube should be premeasured before placement.



Figure 30.7. The oral cavity of a dorsally recumbent Wahlberg's epauletted fruit bat (Epomorphorus wahlbergi) before endotracheal intubation. The tongue is pulled dorsally. The epiglottis lies just beyond the opening in the soft palate.

probe. Arterial blood samples can be collected from the ulnar artery on the medial surface of the humerus.

Body Temperature The thermoneutral zone is for setting environmental temperatures for captive bats. This is the ambient temperature range in which a resting, fasting animal consumes the least amount of oxygen. Within this range, an animal can maintain a constant body temperature without additional energy cost. For large flying foxes (500–1,000 g), the thermoneutral zone lies between 24°C and 35°C, whereas for a lightweight bat such as *Saccopteryx bilineata* (7 g) it is restricted to 30°C to 35°C.

Bats die quickly if the ambient temperature is above body temperature, particularly if the humidity is high. Their only means of lowering body temperature are evaporative cooling and the creation of convection currents by air movement. Flying foxes roost in large trees, often in full sun. As the ambient temperature rises they initially start fanning the air with bent wings. If the ambient temperature approaches body temperature, they wet their fur with saliva and urine and pant, but they cannot sweat. Microchiropterans and smaller Megachiropterans avoid intense heat through their choice of diurnal roosts. Caves, crevices, and hollow trees are ideal, thermally stable environments with temperatures in or near the thermoneutral zone. Because the bats only fly out at night, they never run the risk of overheating. Since most bats roost in sites with localized climates, preferred roost humidity is likely to be greater than 30%, and may approach 100%. Humidity is an important influence on the elasticity of the patagium and very dry conditions are associated with dry membranes.

A temperature probe is placed in either the rectum or esophagus; the latter is preferred because it reflects core body temperature. Rectal temperatures in healthy animals may be as low as 35°C.

Metabolic Hypoglycemia is very likely to occur in the perianesthetic period, particularly in very small, anorectic animals (Widmaier and Kunz, 1992). Blood glucose levels should be maintained above 80 mg/dl.

Supportive Care

To prevent hypothermia, the wings are folded to the body, and the animal is placed on a circulating water blanket. When possible the bat is wrapped in either a blanket or bubble wrap. Alternatively, a commercial forced air warmer developed for human surgery is used. Electric and chemical heating pads are avoided because they cause severe burns to the wing membranes.

Recovery

For recovery, bats are wrapped in a towel and left in a quiet cage to prevent struggling and wing flapping; the animals are usually sufficiently recovered when they are able to crawl out. Alternatively, once gripping returns the bat is suspended from its perch.

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31

Prosimians

Cathy V. Williams and Randall E. Junge

INTRODUCTION

The group of primates referred to as prosimians or strepsirhine primates include lemurs, lorises, pottos, and bush babies. All lemurs are endemic to the island of Madagascar. Under current classification there are five families and nearly 50 separate species of lemurs recognized, although taxonomic groupings continue to change as more information on their genetics becomes available. Lorises, pottos, and bush babies are small bodied, nocturnal primates. Lorises are native to Southeast Asia and India, whereas pottos and galagos are endemic to Africa (Rowe, 1996).

When using anesthetic agents in prosimians it is important to remember that there are very little controlled data on the pharmacokinetics of any drug class in these species. The information contained in this chapter is predominantly derived from the authors' personal experiences and the few published reports that mention use of a particular drug without apparent side effects. Thus, the doses provided here may not be the most pharmacologically appropriate, and there is no guarantee the drugs are entirely safe even though problems have not been documented. It is important to use all drugs conservatively in this group and monitor animals' physiological and behavioral responses carefully to minimize complications.

Prosimians are a very diverse group of primates and physiological responses to a particular drug may vary by species. It is unknown if prosimians respond to anesthetic agents in a manner similar to other primates, but in most instances studies performed in anthropoid primates are the best resource from which to derive information when extrapolating drug doses. The reader is referred to the chapter in this book on primate anesthesia and to selected references for more extensive information on the pharmacological action of anesthetic agents particular to higher primates (Popilskis and Kohn, 1997; Horne, 2001).

SPECIAL PHYSIOLOGY

Prosimian primates exhibit considerable anatomical and physiological variation (Mittermeier, 1994; Rowe, 1996; Sussman, 1999). Size ranges from 25 g for the smallest mouse lemur (Microcebus myoxinus) to more than 7 kg for some members of the Indridae family; diademed sifakas (Propithecus diadema) and indri (Indri indri). Table 31.1 gives approximate adult weight ranges for a variety of prosimian species. Prosimians have a low basal metabolic rate compared with other primates (Ross, 1992). Several behaviors exhibited by lemurs, such as basking and huddling, are related to energy conservation and thermal regulation. Dwarf lemurs (Cheirogaleus sp.) and mouse lemur (Microcebus sp.) are unique among primates in that they hibernate or undergo periods of torpor, an adaptation that allows them to conserve energy during periods of reduced food and water availability (Hladik, Charles-Dominique, and Petter, 1980; Schmid, Ruf, and Heldmaier, 2000).

The body temperature of lemurs and bush babies generally ranges between 97°F to 99°F; however, dwarf and mouse lemurs undergoing torpor may have temperatures significantly below 90°F (Schmid, Ruf, and Heldmaier, 2000; Dausmann et al., 2005). The rectal temperature of lorises is slightly lower than that of lemurs and bush babies and ranges from 95°F to 97°F at normal room temperatures (Whittow et al., 1977; Müller, 1985).

Prosimians have no active mechanism for cooling such as sweating or panting and temperature regulation is accomplished primarily by limiting activity and seeking cool locations during hot weather. Therefore, capture and handling during warm weather should be done either early in the morning while outdoor ambient temperatures are cool or indoors in temperature-controlled environments.

The amount of time necessary to withhold food prior to anesthesia varies by species due to differing

Table 31.1. Body weight ranges for various prosimian species.

Scientific Name	Common Name	Adult Weight (kg)	
Microcebus	Mouse lemur	0.025-0.090	
Loris tardigradis	Slender loris	0.15-0.25	
Mirza coquereli	Coquerel's dwarf lemur	0.028-0.380	
Galago moholi	Southern lesser bush baby	0.15-0.25	
Cheirogaleus medius	Fat-tailed dwarf lemur	0.16-0.25	
Nycticebus pygmaeus	Pygmy loris	0.35-0.45	
Nycticebus coucang	Slow loris	0.80-1.30	
Otolemur crassicaudatus	Thick-tailed greater bush baby	0.70-0.85	
Perodicticus potto	Potto	0.85-1.60	
Eulemur mongoz	Mongoose lemur	1.4-1.6	
Eulemur fulvus	Brown lemur	2.0-2.7	
Eulemur macaco	Black lemur	2.0-2.5	
Eulemur coronatus	Crowned lemur	1.5-2.0	
Lemur catta	Ring-tailed lemur	2.0-3.0	
Varecia sp.	Ruffed lemur	3.0-4.0	
Hapalemur sp.	Bamboo lemur	0.75-2.50	
Propithecus verreauxi coquereli	Coquerel's sifaka	3.3-4.5	
Avahi	Wolly lemur	1.0-1.5	
Indri indri	Indri	6.00-7.25	
Lepilemur	Sportive lemur	0.5-1.0	
Daubentonia	Aye-aye	2.5-3.0	

rates of gastric emptying. Although all prosimians have simple stomachs, the size and conformation of the cecum and large bowel varies depending on the dietary profile of the species. Campbell, Williams, and Eiseman (2004) measured gastric emptying times in four species of lemurs. Gastric emptying times ranged from 3 to 4 hours in the ruffed lemur (*Varecia variegata*), a frugivorous species, and up to 24 hours in eastern lesser bamboo lemurs (*Hapalemur griseus*) and Coquerel's sifaka (*Propithecus verreauxi coquereli*), species that are highly folivorous. The brown lemur (*Eulemur fulvus*), a generalist feeder, had gastric emptying times of 8 hours. Thus, although withholding food for 8 hours is sufficient for the majority of lemur species, longer periods of fasting are likely necessary for highly folivorous species.

RESTRAINT

Physical restraint of prosimians weighing less than 4 kg is relatively simple. Animals less than 1 kg are restrained by grasping over the back of the neck and around the mandible with a gloved hand to control the head and using a second hand to control the lower abdomen and back legs. For animals weighing between 1 and 4 kg, the animal is first netted in its enclosure or out of a transport kennel. The head is initially controlled by placing one hand around the back of the neck and under the jaw to secure the animal. The second hand is then placed under the neck and mandible to prevent serious bites. The animal is allowed to grasp the handler's arm with front and back limbs. Limited exams and minor treatments such as the administration of subcutaneous fluids or SC or IM injections can be performed with

animals in this position (Figure 31.1). When manually restraining lemurs it is recommended that the handler wear arm guards to protect against scratches when animals grasp the handler's forearm. If more control is needed, a second handler is employed to restrain the hind limbs and extend the hind legs while the animal is positioned on its back (Figure 31.2). It is important that the person restraining the hind legs grasp the thighs above the stifles to prevent injury to the knee joint. Although it is possible for experienced handlers to physically restrain lemurs weighing more than 5 kg, the larger species are usually anesthetized for procedures.

VASCULAR ACCESS SITES

Several standard sites are accessible in prosimians; however, the preferred site depends on the species, the size of the animal, and whether it is under manual or chemical restraint. Blood can be collected from the cephalic, external saphenous, and jugular veins, and from the femoral artery or vein. Peripheral veins such as the cephalic and caudal saphenous tend to collapse easily, making withdrawal of more than minimal amounts of blood difficult from these sites. The authors prefer the femoral site for blood collection requiring more than 0.5 to 1 ml of blood. With the animal in dorsal recumbency, the pulse of the femoral artery is palpable in the femoral triangle. The femoral vein lies immediately adjacent and medial to the femoral artery. In most cases the close approximation of the vessels means that the artery is sampled nearly as often as the vein. The main disadvantage with using this site for blood collection is the increased risk of hematoma formation if the artery is



Figure 31.1. Single handler technique for manual restraint of lemurs weighing 1 to 4 kg.



Figure 31.2. Two handler technique for manual restraint of lemurs for physical examination or collection of blood and urine.

sampled and inadequate attention paid to ensuring proper hemostasis after needle withdrawal. This is particularly true in animals that are manually restrained, as blood pressure can be substantially higher than in animals under chemical restraint. In extreme cases, lemurs have died from exsanguination secondary to inadequate hemostasis following blood sampling from the femoral artery.

For indwelling catheter placement in lemurs the external saphenous vein is most accessible; however, the cephalic and jugular veins can be used in larger species.



Figure 31.3. Route of the external saphenous vein on the caudal aspect of the tibia and positioning for occlusion of the proximal venous return in a ring-tailed lemur.

When placing a catheter in the caudal saphenous vein, position the animal in ventral recumbency with the hind legs extended behind the animal. After shaving and preparing the skin of the caudal aspect of the tibia an assistant grasps the caudal thigh of the hind leg and places his or her thumb horizontally across the mid to lower thigh, thus closing off the proximal return of the external saphenous vein. The route of the external saphenous vein is visible along the posterior aspect of the tibia (Figure 31.3).

ENDOTRACHEAL INTUBATION

Endotracheal intubation is relatively straightforward in most prosimians but can be challenging in the smaller species and in aye-ayes. In lemurs, the epiglottis is long and points dorsally completely obscuring visualization of the glottis. With the animal in sternal recumbency the tongue is grasped and pulled forward to visualize the epiglottis. A small blade laryngoscope is useful to aid visualization and move the epiglottis out of the way to expose the glottis. When inserting the endotracheal tube, direct the tube toward the ventral aspect of the glottis. Prosimians, like other primates, have a short trachea. Care must be taken to avoid inserting the endotracheal tube too far and thus intubating a mainstem bronchus. Measuring the length of the endotracheal tube relative to the animal prior to intubation is advised. Once the tube is in place, auscult both sides of the chest for air sounds and monitor end-tidal CO₂ by capnography whenever possible. Cuffed endotracheal tubes ranging in size from 3.0 to 4.5 mm are suitable for animals weighing between 1.5 and 5 kg, whereas uncuffed 2.5 mm Murphy tubes can be used for individuals ranging in size between 750 g and 1.5 kg. For animals weighing less than 1 kg, infant feeding catheters or urinary catheters can be used as endotracheal tubes (Morris, 1997).

Several anatomical variations make aye-ayes (*Daubentonia madagascariensis*) particularly challenging to intubate. The heavy musculature of the jaws prevents the mouth from opening wide and the long upper and lower incisors obscure visualization of the caudal oral and pharyngeal cavities. Intubation of this species is most easily performed by first inserting an 8-10 Fr plastic urinary catheter into the trachea, then passing an endotracheal tube over the urinary catheter into the trachea. Once the endotracheal tube is in place the urinary catheter is removed.

PRE-ANESTHETIC CONSIDERATIONS

As with any animal, disease or abnormalities that alter metabolic pathways or gas exchange affect the safety of anesthesia in prosimian primates. It is important to do a thorough pre-anesthetic evaluation prior to using anesthetic agents. The ease of manual restraint in prosimians makes it possible to perform limited examinations and even draw blood without chemical immobilization in many cases. However, if chemical immobilization is required, careful selection of agents, using the minimum dosage necessary to accomplish the procedure, improves safety.

When developing a pre-operative regimen it is important to consider the analgesic potential of drugs under consideration. Analgesia is most effective when provided preemptively and the administration of analgesics pre-operatively decreases the amount of drugs needed to manage pain post-operatively and may lessen the amount of anesthetic needed by blunting pain perception during the procedure.

It is not always possible to give pre-anesthetic medications but when possible, their administration provides a smoother induction, a more stable plane of anesthesia, and decreases the amount of other drugs needed to produce general anesthesia. Non-steroidal anti-inflammatory drugs (NSAIDs), benzodiazepines, α_2 -agonists, and opioids, have all been used in prosimians successfully. Each can be combined with other drugs to take advantage of the synergistic effects of using drugs that have differing mechanisms of action. Dosages of anesthetic agents commonly used in prosimians are given in Table 31.2.

NSAIDs have no inherent sedative qualities; however, their analgesic effects make their use beneficial peri-operatively as well as for the management of acute and chronic pain not associated with surgery. NSAIDs used in prosimians without obvious side effects include acetaminophen, aspirin, ibuprofen, naproxen, and flunixin meglumine (Table 31.3). As a class cyclooxygenase inhibitory NSAIDs may be associated with gastrointestinal and renal toxicity. All animals receiving NSAIDs should be closely monitored for signs of gastric ulceration or bleeding. The use of parenteral fluids during surgery should be considered when using NSAIDs peri-operatively in animals with known or suspected compromise in renal function.

Benzodiazepines are beneficial premedication agents owing to their anti-anxiety, sedative, and muscle relaxant effects, and for anti-seizure activity. Diazepam and

Table 51.2.	Drugs commonly	used for sedation and anestnesia in	prosimian primates.

Agent	Dosage (mg/kg)	Route	Duration	Reversala
Diazepam	0.5-2.5	IV	30 min	Flumazenil
Midazolam	0.1-0.3	IM	30 min	Flumazenil
Buprenorphine	0.01-0.02	SC, IM, IV	8–12 hr	Naloxone
Morphine	1.0-2.0	PO, SC, IM, IV	3-4 hr	Naloxone
Butorphanol	0.1-0.4	IM	3-4 hr	Naloxone
Medetomidine	0.03-0.06	IM	30-60 min	Atipamazole
Ketamine	5-15	IM, IV	30 min	None
Tiletamine/ zolazepam	3–5	IM		None/Flumazenil
Propofol	3-6	IV	10-15 min	None

^aDoses for reversal agents: atipamizole (0.2 mg/kg IM); naloxone (0.02 mg/kg IM); flumazenil (0.02 mg/kg IV).

Table 31.3. Doses of non-steroidal anti-inflammatory drugs used in prosimian primates.

Agent	Dosage (mg/kg)	Frequency	Route
Acetaminophen	10-15	q 8–12 hr	PO
Aspirin (Acetyl salicylic acid)	10-20	q 8–12 hr	PO
Ibuprofen	10	q 8–12 hr	PO
Naproxen	10	q 12 hr	PO
Ketoprofen	2 mg/kg first dose, then 1 mg/kg daily	q 24 hr	PO, SC, IM, IV
Flunixin meglumine	0.25-0.50	q 24 hr	SC, IM, IV

midazolam have similar pharmacological actions; however, midazolam has advantages over diazepam in exotic species in that it can be given IM, whereas diazepam must be given IV to be effective. When used alone in lemurs, midazolam provides minimal or no detectable sedation; however, when used in conjunction with ketamine for induction, muscle relaxation is improved and the likelihood of seizures is reduced. The authors frequently use midazolam in combination with medetomine prior to induction with gas anesthesia. The combination produces a moderate level of sedation increasing the ease of handling during mask induction.

Information on the physiological response of prosimians to opioids is limited. Butorphanol has been shown to cause profound respiratory depression in primates. This is largely owing to the fact that in primates, butorphanol's effect on the µ receptor is one of a strong agonist rather than the weak agonist or antagonistic as seen in domestic species (Butelman et al., 1995). Whether butorphanol has the same respiratory depressant effects in lemurs or other prosimians is unclear. Studies in ring-tailed lemurs (Lemur catta) using butorphanol at 30 µg/kg IM in combination with medetomidine and ketamine, or medetomidine and midazolam to provide complete anesthesia resulted in only mild decreases in respiratory rates relative to animals receiving no butorphanol. Oxygen-hemoglobin saturation, end-tidal CO₂, and PaCO₂ values were not affected, suggesting oxygenation was not compromised. Butorphanol is used by the authors routinely both for short-term analgesia and as a pre-medication prior to inhalation anesthesia in lemurs; however, until more data are available on receptor activity in this group of primates it is recommended that respiratory parameters are monitored.

The authors routinely use buprenorphine for relief of moderate pain post-operatively with good results. Buprenorphine can be combined with an NSAID, such as ketoprofen, to provide stronger analgesia for moderate to severe pain.

Although there are no references for the use of morphine or fentanyl in prosimians, it is reasonable to expect that these agents can be employed safely if used judiciously and animals are appropriately monitored.

 α_2 -Agonists are very useful in prosimians both for their sedative and analgesic qualities and as a means of decreasing the amount of other anesthetic agents needed. The α_2 -agonist, medetomidine, is one of the few agents studied in lemurs. Medetomidine administered IM to ring-tailed lemurs under isoflurane had no effect on heart rate, blood pressure, or oxygen-hemoglobin saturation (Williams et al., 2003). In contrast, bradycardia occurs in most domestic animals as a compensatory response to rapid and intense vasoconstriction that results in significant hypertension (Cullen, 1996; Paddleford, 1999). Medetomidine combined with midazolam is frequently used at the Duke University Primate

Center for pre-medication prior to inhalation anesthesia. The use of medetomidine pre-operatively substantially decreases the amount of isoflurane and reduces the degree of hypotension seen when isoflurane is used alone.

INDUCTION AGENTS

Ketamine is a widely used anesthetic agent in primates for chemical restraint. The effect of ketamine on prosimians, however, is variable. There are both species and individual differences in the degree and duration of immobilization, character of recovery, and frequency of side effects. When used alone, ketamine provides unpredictable levels of immobilization, poor muscle relaxation, and frequent vomiting on recovery. In the authors' experience, seizures are common in ruffed and black lemurs even at doses of 5 to 10 mg/kg IM. Side effects of ketamine are diminished and the quality of anesthesia is improved when it is combined with either midazolam or medetomidine; however, the duration of effective immobilization remains short at only 10 to 15 minutes.

Telazol, a combination of tiletamine and zolazepam, is frequently used in lemurs, particularly for field immobilizations. Benefits of using Telazol include a wide margin of safety, good muscle relaxation, and smooth recoveries. The main disadvantages include prolonged recovery times in the range of 2 to 6 hours and a short shelf life of the reconstituted drug. In a clinical setting, injectable combinations that can be reversed allow more control over recovery time and depth of anesthesia.

Combining medetomidine with either ketamine and butorphanol, or midazolam and butorphanol, produces heavy sedation to complete immobilization lasting from 20 to 60 minutes (Williams et al., 2003). Both combinations can be used for induction prior to gas anesthesia or as complete injectable regimes. The combinations produce minimal cardiorespiratory effects and the level of analgesia is sufficient to perform minor surgical procedures. Members of the Eulemur genus (brown and black lemurs) tend to require higher doses of the drug combinations than ring-tailed lemurs, ruffed lemurs, and Coquerel's sifaka (Propithecus verreauxi coquereli) to produce equal effects. When mild to moderate sedation is desired as a pre-medication or to increase the ease of handling during manual restraint, administering medetomidine in combination with midazolam is effective. Table 31.4 lists several useful combinations.

Propofol is an injectable alkyl phenol that acts similarly to the ultra-short-acting barbiturate, thiopental. Propofol can be used to provide short duration immobilization for diagnostic procedures or as a constant rate infusion to achieve a light plane of anesthesia for longer periods (Short and Bufalari, 1999). Because the compound must be administered intravenously it is generally impractical to use for induction in prosimians unless animals receive pre-medications in advance.

Table 31.4. Osciul illilliophization regimes for prosimian primati	Table 31.4.	Useful immobilization regimes for prosimian primate
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Drug Combination	Dosage (mg/kg)	Duration of Effect (min)	Level of Sedation
Medetomidine/	0.04	30-40	Light to moderate sedation
Midazolam	0.2		
Medetomidine/	0.04	10-20	Heavy sedation to complete
Ketamine	3–5		immobilization
Butorphanol/	0.4	15-30	Complete immobilization
Medetomidine/	0.04		*
Ketamine	3–5		
Butorphanol/	0.4	20-50	Complete immobilization
Medetomidine/	0.04		-
Midazolam	0.2-0.3		

Propofol decreases cardiac contractility and is a potent vasodilator that can result in hypotension. It is also a respiratory depressant. Administering propofol slowly and to effect minimizes the occurrence of cardiopulmonary effects. The quality of induction and the rapid rate of metabolism, and hence recovery, make the use of propofol advantageous in some circumstances.

INHALATION ANESTHESIA

Isoflurane works well and is safe on most species; however, respiratory arrest is common in Coquerel's dwarf lemurs (Mirza coquereli) induced with isoflurane and the agent should be avoided in this species until more information is available. Isoflurane is a potent vasodilator and hypotension is frequently observed in prosimians anesthetized with this agent. It is important to monitor blood pressure in animals under isoflurane anesthesia and be prepared to administer IV fluids or other supportive measures as necessary to maintain adequate blood pressure. Information is not available regarding the mean alveolar concentration (MAC) of isoflurane in prosimians; however, it is the authors' impression that MAC may vary by species. Aye-ayes, in particular, seem acutely sensitive to isoflurane and require lower concentrations relative to other lemur species to achieve a surgical plane of anesthesia. Marked hypotension unresponsive to fluid administration alone is a frequent complication of isoflurane use in aye-ayes even at very low doses. Until more information is available it is advisable to keep anesthetic events in aye-ayes as short as possible and intensively monitor cardiopulmonary function.

Prosimians can be easily induced with gas anesthetics via face mask or induction chamber. Administering pre-medication improves the quality of mask induction with isoflurane. Sevoflurane may offer advantages over isoflurane for mask induction as it has a non-irritating odor and induction rates are faster owing to very low blood and tissue solubility. The cardiopulmonary effects of sevoflurane are similar to isoflurane (Clark, 1999).

MONITORING

All anesthetic agents have the potential to adversely affect the major organ systems of the body. Body temperature, heart rate, and rhythm, respiratory rate, and capillary refill time can be monitored in even the smallest lemur or loris. With experience and the proper equipment evaluating cardiac electric activity (ECG) and obtaining reliable readings for oxygen-hemoglobin saturation (pulse oximetry), end-tidal $\rm CO_2$ (capnography), and blood pressure (oscillotometry) can be accomplished reliably in patients weighing more than 1.5 kg. Monitoring should start in the pre-operative phase and continue until the animal is in sternal recumbency or safety precludes further measurements.

Lemurs are highly prone to developing hypothermia under anesthesia owing to their lean body confirmation and high surface area to body mass ratio. Heat loss is further compounded by shaving and wetting the remaining hair during aseptic preparation of the surgical site. Opening a body cavity further enhances the loss of body heat. Hypothermia decreases liver and renal blood flow and slows the elimination of anesthetic agents, prolonging recovery (Sessler, 2000). It is important to monitor temperature regularly during anesthetic procedures. Esophageal thermometers more accurately monitor core body temperatures than rectal thermometers (Lumb and Jones, 1984). Heat loss can be minimized by insulating animals from cold surfaces by using warm water circulating blankets or heated surgical tables and minimizing exposure by covering areas outside of the surgical field. Additional precautions include warming surgical skin preparation solutions and supplemental fluids for intravenous support or lavage.

Blood pressure can be measured directly by arterial catheterization or indirectly using either Doppler sphygmomanometry or automated oscillotonometry. In the majority of instances, the authors find that automated oscillotonometry units made for small companion animals are easy to use and provide reliable readings in animals over 1.5 kg. The cuff is placed on the hind leg just above the tarsal joint. Additional sites for cuff placement

in animals weighing more than 3 kg include the base of the tail and the upper forearm close to the axilla. It is important to maintain the mean arterial pressure (MAP) above 60 mmHg to ensure adequate tissue blood flow.

Pulse oximetry can be challenging in prosimian primates. Their tongues are short and thin and probes tend to slip off easily. Several lemur species have heavy pigmentation of the tongue, mucous membranes of the oral cavity, and skin of the hands and feet, making readings inconsistent and difficult to obtain. In lightly pigmented animals reliable readings can generally be obtained by placing a fingertip probe on the cheek wall. In heavily pigmented animals rectal readings using a rectal probe are more reliable. To ensure proper placement of the rectal probe place the animal in dorsal recumbency and direct the probe signal toward the dorsal wall of the rectum. Manual evacuation of feces in the rectum avoids trapping of feces between the probe and rectal mucosa, which interferes with signal transduction.

The use of capnography in prosimians is similar to that in other small animals. Capnography provides important information on cardiac function and pulmonary perfusion. The end-tidal CO_2 level is a measure of the amount of CO_2 present in expired air. For more information on the use of capnography and interpretation of end-tidal CO_2 measurements the reader is referred to papers describing their use in veterinary patients (Grosenbaugh, 1998; Marshall, 2004).

Arterial blood gas analysis is the most reliable method of assessing pulmonary function. The development of relatively inexpensive hand-held analyzers makes measuring blood gases possible and practical, even in field settings. In prosimians, arterial blood samples are easiest to obtain from the femoral artery. Hemoglobin is nearly saturated at PaO₂ levels of 80 mmHg; however, animals breathing 100% oxygen can have significantly higher values. Patients with PaO₂ levels between 60 and 80 mmHg are moderately hypoxemic, and values below 60 mmHg are indicative of severe hypoxemia.

RECOVERY

The quality and speed of recovery depend on the agent used, the general health of the animal, and the success of maintaining physiological processes within optimal ranges through the use of monitoring and appropriate supportive care. Pre-medication with a variety of agents may prolong time to extubation. Reversible agents allow smooth and controlled recovery from anesthesia. Providing supplemental heat during recovery is beneficial for animals in which body temperatures drop during anesthetic procedures. Animals should be prevented from attempting to climb or jump until well coordinated. Allowing recovery to occur in a confined space, such as a pet carrier, is helpful.

REMOTE IMMOBILIZATION AND FIELD TECHNIQUES

Remote immobilization of lemurs is routinely performed in the field; however, the safety of the procedure is related to the skill of the darter, the type of darting equipment used, and the extent to which animals are monitored during immobilization. Lemurs present a difficult target, particularly when high up in a tree. Lemurs have a lean body conformation and safe sites for dart placement are limited. The caudal thigh muscles provide the safest location to dart lemurs. Because of lemurs' small size and minimal muscle mass low impact delivery devices such as blow guns are the least traumatic and provide the greatest margin of safety when darting. However, with experience and appropriate caution, CO₂-powered remote injection devices that allow downward adjustment of the discharge power can be used successfully.

Dissociative anesthetics are the most frequently used class of drugs for field immobilizations in lemurs. Telazol is widely used and provides rapid induction, good muscle relaxation, and a wide margin of safety. The main disadvantage is a long recovery time, in the range of 4 to 6 hours. Published doses for Telazol used in lemurs in the field vary from 10 to 20 mg/kg (Glander et al., 1992; Dutton, Junge, and Louis, 2003; Junge and Louis, 2005). In the authors' experience, 10 mg/kg provides excellent immobilization and relaxation for most field procedures, producing 30 to 40 minutes of immobilization. It is much safer to administer supplemental doses of 2 to 3 mg/kg IM if longer immobilization is required than to increase the occurrence of complications and prolonged recoveries that occur with higher doses.

Ketamine at doses of 17 to 50 mg/kg (Richard, Rakotomang, and Schwartz, 1991; Glander et al., 1992; Garell and Meyers, 1995) has been used for field immobilizations in lemurs but the results are generally inferior to those produced with Telazol. Ketamine immobilizations are typically plagued by poor muscle relaxation, unpredictable levels of restraint, and rocky recoveries. Vomiting on recovery is common.

Medetomidine is a useful adjunct to dissociative anesthetics in the field. Administering medetomidine in place of supplemental doses of Telazol or ketamine increases the duration and improves the depth of anesthesia without prolonging recovery time. In animals initially immobilized with Telazol, the authors find that the administration of 40 μ g/kg of medetomidine IM provides approximately 30 minutes of additional immobilization. Medetomidine administered IM immediately following darting with ketamine improves muscle relaxation and produces better immobilization than when ketamine is used alone (M. Sauther, personal communication). The ability to reverse medetomidine is a distinct advantage in a field setting. As in clinical settings, proper monitoring is critical.

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32

Monkeys and Gibbons

Rolf-Arne Ølberg

INTRODUCTION

Primates are found wild, as well as in research facilities, zoos, and as pets. Anesthesia is essential in most instances for medical examination and treatment. Some are anesthetized for other reasons, such as relocation or identification.

TAXONOMY AND BIOLOGY

Monkeys belong to the suborder *Haplorhini* (higher primates), which, excluding great apes and humans, contains five families and over 200 species (Table 32.1). The *Tarsiidae*, *Cercopithecidae*, and *Hylobatidae* families are Old World primates from Africa or Asia, whereas the *Callitrichidae* and *Cebidae* are New World primates from the neotropics.

Tarsiers are small nocturnal insectivorous species; they can turn their head 360 degrees and some can leap as far as 5 to 6 m between trees. Callitrichids (marmosets and tamarins) are small, diurnal, and live in family groups. They have good eyesight and hearing, and are usually active and agile. Their thumbs are not apposable and they have clawlike nails on all digits except the toes. Cebids (Cebidae) vary in weight from 1 to 15 kg and many have prehensile tails. Most are good jumpers and runners. The Cercopithecidae all have longer hind limbs than forelimbs, none have prehensile tails, and they range in weight from 1 to 55 kg. The upper canines are elongate, whereas the lower are curved slightly inward and backward. The Hylobatid primates include the gibbons and siamangs. They have relatively long arms, and can leap from branch to branch for distances up to 9 meters or more. They are monogamous, strongly territorial, lack a tail, have long canine teeth and weight 4-13 kg. For an extensive description of the various species, the reader is referred to Walker's Mammals of the World (Nowak, 1999).

PHYSIOLOGY

Primates have a large surface-area-to-body mass ratio; consequently, rapid body heat loss commonly occurs during anesthesia. This is compounded by drug suppression of hypothalamic thermoregulation and impairment of shivering. Heat loss is most pronounced in small species.

There are few reports of reference ranges for primate heart rate, respiratory rate and blood pressure. Heart rates are approximately 100 to 200 beats per minute (bpm) for animals weighing greater than 1 kg, and 200 to 300 bpm for primates weighing less than 1 kg (Bourne, 1975; Johnson-Delaney, 1994; Haruo, 1995). The respiratory rate is 20 to 50 breaths per minute for most species. These physiological reference ranges are altered by anesthesia or restraint (Bush et al., 1977; Liu and DeLauter, 1977).

HUMAN SAFETY

Most primates deliver a nasty bite when restrained or confined that may transmit several zoonotic pathogens. Herpes B virus is endemic and non-pathogenic in macaques, but can be fatal in humans (Hummeler et al., 1959; Ott-Joslin, 1993). Therefore, a primary aim when handling primates is prevention of traumatic injury and transmission of zoonoses to humans.

VASCULAR ACCESS

Common vascular access sites are the femoral and saphenous (popliteal) veins. The femoral vein is entered just distal to the inguinal canal. With the animal on its back and its legs abducted, the pulsing femoral artery is palpated. The femoral vein lies medial to the artery and just under the skin in the triangle formed by the abdominal, sartorius, and pectineus muscles. In small primates (i.e., callitrichids and squirrel monkeys) the vein is

Table 32.1. Taxonomy of monkeys including approximate adult body weights.

Scientific Name	Common Name	ABW (kg)
Family: Tarsiidae		
Tarsius, 5 species	Tarsiers	0.08-0.17
Family:Callitrichidae		
Callimico, 1 species	Goeldi's monkey	0.4-0.9
Saguinus, 12 species	Tamarins	0.2 - 0.9
Callithrix, 17 species	Marmosets	0.2-0.5
Cebuella, 1 species	Pygmy marmoset	0.08 - 0.15
Family:Cebidae		
Lagothrix, 2 species	Woolly monkey	5-11
Ateles, 6 species	Spider monkeys	6-8
Brachyteles, 1 species	Woolly spider monkey	7-10
Alouatta, 9 species	Howler monkeys	4-12
Pithecia, 5 species	Sakis	0.7 - 1.7
Cacajao, 2 species	Uakaris	2.7-3.5
Callicebus, 13 species	Titi monkeys	0.5 - 2.0
Aotus, 10 species	Night monkeys	0.6 - 1.0
Cebus, 6 species	Capuchins	1.1-4.3
Saimiri, 5 species	Squirrel monkeys	0.7-1.1
Family:Cercopethicidae		
Erythrocebus, 1 species	Patas monkey	7-13
Chlorocebus, 4 species	Savannah guenons	2-9
Cercopithecus, 20 species	Guenons	2–12
Miopithecus, 1 species	Talapoin	0.7 - 1.2
Cercocebus, 3 species	Mangabeys	3-20
Lophocebus, 1 species	Black mangabeys	4-11
Macaca, 20 species	Macaques	2-18
Papio, 5 species	Baboons	14-41
Mandrillus, 2 species	Mandrills	12-25
Theropithecus, 1 species	Gelada baboon	13-20
Nasalis, 1 species	Proboscis monkey	7-22
Simias, 1 species	Pig-tailed langur ´	7
Pygathrix, 1 species	Douc langur	
Rhinopithecus, 4 species	Snub-nosed langurs	
Presbytis, 8 species	Langurs	5-8
Semnopithecus, 1 species	Hanuman langur	5-24
Trachypithecus, 9 species	Brown-ridges langurs	4-14
Colobus, 5 species	Black-white colobus	5-15
Piliocolobus, 5 species	Red colobus	5-12
Procolobus, 1 species	Olive colobus	3–5
Family:Hylobatidae		
Hylobates, 11 species	Gibbons and siamangs	4-13

visualized in the inguinal area as a dark line just under the skin. The saphenous (popliteal) vein is located superficially on the caudal aspect of the lower leg. It is suitable for catheter placement in most primates, including callitrichids. Less common vascular access sites include the jugular and cephalic veins. In monkeys with tails the lateral coccygeal veins can also be used. They are palpable on the dorsolateral surface of the base of the tail.

PHYSICAL RESTRAINT

A variety of physical restraint techniques in primates are safe both for the handler and the primate. These include nets, squeeze cages, and head lock devices. However,

any restraint is stressful to the animal and its duration must be minimized (Bush et al., 1977).

Hoop nets are useful for catching smaller species (less than or equal to 10 kg). The animal is physically secured within the net by pinning it to the ground or closing off the entrance by twirling the net. The animal is then moved directly to a transport cage or induction box, injected with an anesthetic drug, or administered inhalant anesthetic through the net using a mask placed over the head.

Manual restraint is excellent for small species (e.g., tamarins and marmosets). These species are caught in a hoop net and then secured by locking the head with thumb and index finger, the upper body with the other three fingers, and the legs with the other hand. This restraint technique is suitable for minor procedures

such as inspection of wounds, to facilitate injection of drugs, and blood sampling. Leather gloves or a towel will reduce bite wounds.

Squeeze cages are indicated for animals too dangerous to handle by hand (i.e., aggressive males or animals greater than or equal to 10 kg). There are many commercial cages available; they are essential for the humane and safe medical and anesthetic management of primates. Once in a squeeze cage, the animal is compressed for intramuscular (IM) injection of a parenteral anesthetic. A properly compressed primate will not be able to move, allowing accurate injection.

PSYCHOLOGICAL RESTRAINT (TAMING)

Taming and training methods are used for "psychologically restraining" animals. This is a common method used for domestic animals such as horses and dogs, but it can also be used on non-domestic animals to facilitate, for example, hand injection of drugs. Through positive reinforcement, many primates will accept an IM injection or extend an arm out of the cage for blood collection (Phillippi-Falkenstein and Clarke, 1992).

ENDOTRACHEAL INTUBATION

Endotracheal intubation is readily achieved in most species with the aid of a laryngoscope and a suitable endotracheal tube. Intubation can be achieved with the primate positioned in dorsal recumbency on a table with the head flexed slightly backward (Figure 32.1). Alternatively, the animal is placed in a sitting position and an assistant flexes the head backward. The tongue is gently pulled outwards to visualize the glottis with a laryngoscope. The use of topical local anesthetic on the glottis will reduce laryngospasm and bucking after intubation.

Primates have a relatively short trachea, with the bifurcation located close to the neck (Figure 32.2). It is easy to place an endotracheal tube too far, intubating a main bronchus and ventilating only one lung (Horne, 2001). To prevent this, the endotracheal tube length is premeasured before placement. Once the tube is in position, the animal is ventilated and both the left and right thorax auscultated. If the tube is located in one bronchus there will be no respiratory noise on the opposite side.

PRE-ANESTHETIC CONSIDERATIONS

Observing the animal prior to the anesthetic procedure will provide useful information about its health status. Social interaction, lethargy, diarrhea, vomiting, anorexia, body condition, and presence of wounds can often be evaluated by observation.

If possible, it is recommended to not feed the primates for at least 12 hours prior to the anesthetic proce-

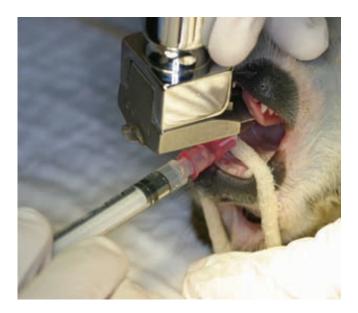


Figure 32.1. Endotracheal intubation in primates, as in this squirrel monkey, is facilitated by placing the animal in dorsal recumbency, extending the head and neck using a laryngoscope, and applying topical anesthetic to the glottis to reduce laryngospasm.



Figure 32.2. The primate trachea is short. The endotracheal tube is premeasured to ensure it does not pass into a major bronchus.

dure. For smaller primates (less than 1 kg) 6 to 8 hours prior to the procedure is recommended, as these animals often have a higher metabolic rate and are more likely to develop hypoglycemia.

A pre-anesthetic health check is most often not possible, but a quick physical examination immediately after induction is recommended. After checking circulation and airway, an accurate body weight, rectal temperature, hematocrit, serum total protein, and urea and creatinine will give useful information about the drug dosage, hydration status, and need for cooling or supplemental heat.

ANESTHESIA

There are now numerous drugs available for anesthesia of primates. Different drugs may be used in various situations, depending on the species being examined, duration of the procedure, and condition of the animal. Sick and compromised individuals may require a different anesthetic drug from that used in healthy individuals. In most instances, preanesthetic evaluation of health status in zoo animals is done exclusively by observation without adequate hands-on evaluation. Therefore, ideally anesthetic drugs should be safe, and reversible with minimal side effects in all primates, even those that are compromised. Unfortunately, there is still no single agent that fulfills all of these requirements. Drugs are commonly used in combinations to increase potency and safety, or better suit the requirements of the procedure. The choice of agent, or combination of agents, usually depends on the experience of the veterinarian and his or her familiarity with a particular agent or drug combination.

There are several options for administering drugs to primates. Drugs can be administered orally, by hand injection, remotely by use of a dart (see Chapter 4), or by inhalation of anesthetic gases.

Oral Route

Drugs are administered orally by squirting into the mouth, or mixing in liquid or solid treats. Ingestion of a drug is a voluntary action, and depends on it being palatable or the flavor being masked by the taste of something else. Numerous attempts have been made to encourage primates to take drugs as tablets or other formulations (Martin et al., 1972; Knottenbelt and Knottenbelt, 1990; Miller et al., 2000; Ølberg, 2004). However, there are no reports of using this as a consistent, safe, and reliable method to anesthetize primates.

Injectable Route

Hand injection requires physical or psychological restraint. Pole-syringes function as an extended hand, but require the animal to be confined to a relatively small space.

For larger species, the use of a projectile dart to deliver drugs is common practice, and darts typically are used for immobilizing primates in the wild (Burroughs, 1993; Sapolsky and Share, 1998) (see Chapter 4). Darting is fast and effective, but has significant disadvantages, including stress, pain, and even trauma on injection. Primates have relatively small target areas for darting and these can be difficult to hit, especially on a moving animal. Targets usually used for injection are the muscles in the hip and thigh area, or, in rare instances, the triceps or shoulder area of larger monkeys.

DRUGS

Several review papers describe anesthesia of primates (Beck, 1972; Martin et al., 1972; Cohen and Bree, 1978;

Sainsbury, Eaton, and Cooper, 1989; Horne, 2001). Most of the literature is based on empirical experience and often reflects subjective evaluation by the authors. There are few prospective studies, and fewer studies critically evaluate cardiopulmonary safety of drugs and dosages. This limits the interpretation of data, drug, and dosage recommendations. Relevant published studies on injectable anesthesia are listed in Table 32.2.

Most drug combinations include a dissociative anesthetic, alone or in combination with α_2 -adrenoceptor agonists, opioids, or benzodiazepines. Alphaxalone/alphadolone, methohexitone, thiamylal, droperidol, acepromazine, and propofol have been used, but are not included in this chapter. (For more information on these anesthetic agents see Marsboom, Mortelmans, and Vercruysse, 1963; Box and Ellis, 1973; Bowden, Holm, and Morgan, 1974; Reed and Staple, 1976; Connolly and Quimby, 1978; Porter, 1982; Sainsbury, Eaton, and Cooper, 1989; Fowler et al., 2001.)

Although numerous drugs are used and recommended, there are currently no drugs licensed specifically for primates. Therefore, the use of these drugs must be considered extra label.

Dissociative Anesthetics

Phencyclidine was commonly used in the 1960s and 1970s (Beck, 1972; Krahwinkel, 1972; Cohen and Bree, 1978; Martin et al., 1984). However, phencyclidine has severe side effects, such as rough prolonged recoveries with hallucinations and extrapyramidal signs, and is no longer available. Ketamine and tiletamine are used extensively (Gray, Bush, and Beck, 1974; Cohen and Bree, 1978; Schobert, 1987; Jalanka, 1989).

Ketamine A significant advantage of ketamine is its high therapeutic index. It has been used alone as an anesthetic agent (10 to 100 mg/kg) (Martin et al., 1972; Vercruysse and Mortelmans, 1978). It has also been given experimentally to five squirrel monkeys at dosages of 250 mg/kg without any deaths (Greenstein, 1975). It can be administered safely several days in a row for repeated anesthesia (Bree, Feller, and Corssen, 1967). Ketamine causes reliable immobilization, and maintains stable cardiopulmonary function and the laryngeal reflex. However, there are no antagonists. This is a significant disadvantage in case of complications during immobilization or accidental overdosage.

The duration of effect is relatively short (depending on dosage), mainly owing to rapid redistribution from the central compartment. Ketamine is also rapidly metabolized in the liver. The recovery period is prolonged and rough when high dosages are used alone (Banknieder et al., 1978). This might result from emergence delirium, a severe and common side effect in humans (Reich and Silvay, 1989), which occurs in approximately 5% to 30% of cases (White, Way, and Trevor, 1982). This state is associated with visual,

 Table 32.2.
 Drug dosages used for anesthesia of primates.

Species	Drug(s)	Dosage (mg/kg)	N	Duration (minutes)	Comment	References
Common marmoset (Callithrix jacchus)	MK	0.1/5.0	7	NA	I-DS	(Jalanka and Roeken, 1990)
	TZ	2.2	1	NA	+ Halothane	(Gray et al., 1974)
White-lipped tamarin (Saguinus nigricollis)	ZL	8.8-9.9	4	NA	Two died, dose too high	(Gray et al., 1974)
Red-bellied tamarin (Saguinus labiatus)	MK	0.1/5.0	1	AZ A	SO	(Jalanka and Roeken, 1990)
Emperor tamarin (Saguinus imperator)	MK	0.1/5.0	11	NA	DS-I	(Jalanka and Roeken, 1990)
Cotton-headed tamarin (Saguinus oedipus)	MK	0.1/5.0	7	NA	DS-I	(Jalanka and Roeken, 1990)
	ZL	2.2	2	NA	CR	(Eads, 1976)
Squirrel monkey (Saimiri sciureus)	ZL	4.4-22	40	NA	CR-SA	(Eads, 1976)
	×	11	4	13	CR	(Greenstein, 1975)
		25	10	20	SA	(Greenstein, 1975)
		50	4	54	SA	(Greenstein, 1975)
		12-30	25	NA	CR-SA	(Beck and Dresner, 1972)
Owl monkey (Aotus trivirgatus)	×	10-25	41	NA	CR-SA	(Beck and Dresner, 1972)
Black-handed spider monkey (Ateles geoffroyi)	TZ	2.2-8.8	23	NA	CR-SA	(Eads, 1976)
Black spider monkey (Ateles fusciceps)	X	9.6-28.7	20	28-45	I	(Bush et al., 2001)
	ZZ	1.8-5.0	7	22–34	Ι	(Bush et al., 2001)
		2.7-9.3	23	NA	CR-SA	(Eads, 1976)
Black spider monkey (Ateles chamek)	ZL	11.6–18.7	8	NA	I	(Karesh et al., 1998)
Woolly monkey (Lagothrix lagothricha)	TZ	3.3-8.8	24	NA	CR	(Eads, 1976)
White-throated capuchin (Cebus capucinus)	TZ	3.3-11.0	11	NA	CR-SA	(Eads, 1976)
Black howler monkey (Alouatta caraya)	ZZ	2.9-4.4	3	NA	CR	(Eads, 1976)
	×	0.9	099	20	I	(Colillas, 1978)
Red howler monkey (Alouatta seniculus)	MK	0.15/4.0	63	31–48	I	(Vie et al., 1998)
	TZ	22 adults	44	40–50	I	(Agoramoorthy and Rudran, 1994)
		30 juveniles	9	06	I	
Mantled howler monkey	ZL	3.1-4.8	4	27–34	I	(Bush et al., 2001)
(Alouatta palliata/villosa)						
Cynomolgus macaque (Macaca fascicularis)	×	12-25	48	NA	CR-SA	(Beck and Dresner, 1972)
	\times	10	9	21–41	A	(Young et al., 1999)
	ZL	2.5-20.0	1528	NA	CR-SA	(Eads, 1976)
	MK	0.05/2.0	9	25-32	U-A	(Young et al., 1999)
Lion-tailed macaque (Macaca silenus)	\times	9.2–13.8	11	21–44	I	(Bush et al., 2001)
	ZZ	2.2-4.4	15	NA	CR-SA	(Eads, 1976)
	ZI	2.5-2.7	3	23–29	I	(Bush et al., 2001)
Barbary macaque (Macaca sylvanus)	×	11.0-18.2	12	26-72	Ι	(Bush et al., 2001)
	ZI	2.2-4.3	3	28-35	Ι	(Bush et al., 2001)
		2.2-4.4	28	NA	CR	(Eads, 1976)
Pig-tailed macaque (Macaca nemestrina)	X	9.2–10.7	3	20–38	I	(Bush et al., 2001)
	ZZ	2.2-19.3	26	NA	CR-SA	(Eads, 1976)
Rhesus macaque (Macaca mulatta)	×	10	5	55	A	(Banknieder et al., 1978)
	\times	11/0.55	12	28–94	A	(Connolly and Quimby, 1978)
	XK					
		9.0/2	2	100	A	(Banknieder et al., 1978)
	ZZ	5.0/1.0	2	53-71	A	(Naccarato and Hunter, 1979)
		2.2-22.0	177	ZA	CR-SA	(Eads, 1976)
						(Consistano)

(Continued)
32.2.
Table

Species	Drug(s)	Dosage (mg/kg)	Ν	Duration (minutes)	Comment	References
Japanese macaques (<i>Macaca fuscata</i>)	K	5.0	2	NA	CR	(Beck and Dresner, 1972)
	M	0.12	9	47 ± 13	Ω	(Miyabe et al., 2001)
	MMid	0.03/3.0	13	74 ± 37	DS-CR	(Miyabe et al., 2001)
Green monkey (Chlorocebus sabaeus)	\times	8.8-19.0	2	20–33	Imm	(Bush et al., 2001)
	ZZ	3.0-6.0	30	NA	SA	(Eads, 1976)
Patas monkey (Erythrocebus patas)	\times	10.0-12.6	2	28–36	Ι	(Bush et al., 2001)
	ZZ	2.2-7.2	13	NA	CR-SA	(Eads, 1976)
	MBK	0.05/0.4/3.0	7	30–50	A	(Kalema-Zikusoka et al., 2003)
	MBMid	0.05/0.4/0.3	7	50	A	(Kalema-Zikusoka et al., 2003)
Black and white colobus (Colobus guereza)	\bowtie	9.0-11.0	9	20–27	Ι	(Bush et al., 2001)
	ZZ	2.1–3.3	4	18–33	Ι	(Bush et al., 2001)
		1.5-4.4	18	NA	CR	(Eads, 1976)
DeBrazza's monkey (Cercopithecus neglectus)	\times	9.4-10.1	3	28–33	Ι	(Bush et al., 2001)
	ZZ	2.8-7.2	10	NA	CR	(Eads, 1976)
Hamadryas baboon (Papio hamadryas)	MK	0.1/5.0	7	NA	I-DS	(Jalanka and Roeken, 1990)
	ZL	1.3	1	NA	CR	(Eads, 1976)
Olive baboon (Papio anubis)	\times	5.0-15.0	16	NA	CR-SA	(Beck and Dresner, 1972)
	KD	10/0.2-0.4	38	NA	A	(Woolfson et al., 1980)
	ZL	2.0-4.0	9	NA	CR	(Eads, 1976)
Yellow baboon (Papio cynocephalus)	\times	5.0-10.0	47	NA	CR-SA	(Beck and Dresner, 1972)
		11.0	9	64-88	A	(White and Cummings, 1979)
	KX	11.0/0.5	9	90-125	A	(White and Cummings, 1979)
	ZZ	6.6 - 11.0	3	NA	CR-SA	(Eads, 1976)
Western baboon (Papio papio)	\bowtie	8.0-20.0	<29	22–85	CR	(Marsboom et al., 1963)
White-handed gibbon (Hylobates lar)	\bowtie	5.0-12.0	6	NA	CR-SA	(Beck and Dresner, 1972)
	ZZ	2.2-4.4	∞	NA	CR	(Eads, 1976)
	MK	0.07/3.0	9	NA	DS	(Jalanka and Roeken, 1990)

CR, Chemical restraint; DS, deep sedation; I, immobilization; K, ketamine, KD, ketamine/diazepam; KX, ketamine/xylazine; N, number of animals in the study; NA, not available; MBK, medetomidine/ butorphanol/ketamine; MBMid, medetomidine/butorphanol/midazolam; MS, medetomidine/ketamine; MMid, medetomidine/midazolam; SA, surgical anesthesia; TZ, tiletamine/zolazepam.

The comment reflects the investigator's description of the anesthetic effect.

All drugs were given IM.

auditory, proprioceptive, and confusional illusions (Stoelting, 1999). The side effect is markedly reduced if ketamine is used in combination with sedative agents such as α_2 -agonists or benzodiazepines (Lilburn et al., 1978; Levanen, Makela, and Scheinin, 1995).

Ketamine has been used alone in a wide variety of primates, and most reports describe it as safe and reliable. Effective intramuscular dosages vary from 5 to 12 mg/kg for chemical restraint, up to 10 to 30 mg/kg for surgical anesthesia (Beck and Dresner, 1972; Ochsner, 1977). Some authors give a general recommendation of dosages from 5 to 40 mg/kg IM (Cohen and Bree, 1978). The variation is mainly size and species related.

The minimum effective IM dosage for black howler monkeys is 6 mg/kg (Colillas, 1978), whereas the suggested initial dosage for the bonnet and cynomolgus macaques is 12 to 15 mg/kg; yet for other macaque species (e.g., the rhesus monkey) 5 to 10 mg/kg is suggested (Beck and Dresner, 1972). Small species generally require a higher dosage than larger species (e.g., squirrel monkey 12 to 15 mg/kg) (Beck and Dresner, 1972).

Induction is normally rapid (3 to 5 minutes) after IM injection. Some suggest that induction time is dose related (Greenstein, 1975), whereas others state it is relatively constant with different dosages, but varies among species (Vercruysse and Mortelmans, 1978). Duration and recovery time is mainly dose-dependant (Vercruysse and Mortelmans, 1978), but there is also a difference in sleep time among species (Domino, McCarthy, and Deneau, 1969). Ketamine has a maximum concentration in aqueous solution of 200 mg/ml.

Tiletamine Tiletamine is only available in combination with the benzodiazepine zolazepam. Plasma half-life in primates is 1 to 1.5 hours. The drug is metabolized in the liver and the two metabolites are excreted in the urine (Lin, 1996).

The lethal dose for primates is 50 mg/kg IV (Lin, 1996), approximately 10 times the effective IM dosage for many primate species.

α₂-Adrenoceptor Agonists

Much of the research on α_2 -adrenoceptor agonists (α_2 -agonists) has been performed in dogs whose physiological responses differ from primates. In both primates and humans, the negative cardiopulmonary effects of α_2 -agonists are minor and not clinically noticeable (Dyck et al., 1993; Horne, Norton, and Loomis, 1997; Capuano, Lerche, and Valverde, 1999). Muscle relaxation is profound because of α_2 -adrenoceptor-mediated inhibition of neurotransmission at the interneuron level of the spinal cord (Cullen, 1996). The α_2 -agonists impair proper function of the central noradrenergic control of thermoregulation, which in some instances can lead to hypothermia or hyperthermia, depending on ambient temperature (Scheinin et al., 1989).

 α_2 -Agonists significantly reduce the dose required of both injectable and inhalation anesthetics (Knight, 1980; Bloor and Flacke, 1982; Ewing et al., 1993). The first signs of sedation (slow and clumsy movements) in stump-tailed macaques were observed after 10 µg/kg medetomidine IM (Rama, Linnankoski, and Carlson, 1997). In rhesus macaques there was no difference in bradycardic, hypotensive, and sedative/analgesic properties measured at medetomidine dosages of 100, 150, and 200 µg/kg IV (Capuano, Lerche, and Valverde, 1999). These authors recommended an IM medetomidine dosage of 50 to 100μ g/kg in combination with ketamine.

The effects of α_2 -agonists are reversed in primates by the α_2 -adrenoceptor antagonists such as atipamezole, yohimbine, tolazoline or idazoxan (Paddleford and Harvey, 1999). The most specific alpha₂-adrenoceptor antagonist, atipamezole, is recommended in primates (Haapalinna et al., 1997; Aantaa, 2000).

Opioids

Opioids are mainly used for analgesia, and the µ receptor agonists are the ones producing the strongest effect, with regard to both supraspinal and spinal analgesia (Atcheson and Lambert, 1994). Analgesia, sedation, and respiratory depression increase with increased plasma concentrations.

Butorphanol is an example of an agonist-antagonist opioid. However, it has significant respiratory depressant effects in primates, related to its effect on μ receptors (Liguori, Morse, and Bergman, 1996), compared with the minimal respiratory depressant effects seen in other animals such as dogs and cats. Minute ventilation in rhesus monkeys is reduced 60% to 75% by butorphanol (0.1–0.3 mg/kg IM).

In rhesus monkeys fentanyl IV produced respiratory depression and analgesia at dosages as low as $2 \mu g/kg$, and apnea was seen consistently at $60 \mu g/kg$ (Nussmeier et al., 1991). There may be large differences in dosage requirements among different species because of variations in concentration and distribution of opioid binding sites (Robson, Gillan, and Kosterlitz, 1985). This difference may be marked when compared with unrelated species, such as dogs, which do not develop apnea even at $3000 \mu g/kg$ IV (Arndt, Mikat, and Parasher, 1984; Bailey et al., 1987).

Naloxone, naltrexone, and nalbuphine are μ opioid receptor antagonists, and effectively displace the agonists from the receptor binding sites, reversing the effects (Stoelting, 1999).

Benzodiazepines

The main clinical effects of benzodiazepines are sedation, anxiolysis, anticonvulsive actions, spinal cord-mediated skeletal muscle relaxation, and anterograde amnesia (Ashton, 1994). Benzodiazepines have few side effects, with a high therapeutic index (Du Plooy et al., 1998). However, these drugs may cause mild respiratory

depression, which may become significant when benzodiazepines are combined with other sedative or anesthetic agents (Gerak, Brandt, and France, 1998). They significantly decrease the minimum alveolar concentration (MAC), or dose, if used in combination with inhalational or injectable anesthetics (Melvin et al., 1982). In clinical doses they have minimal effects on heart rate, cardiac output and contractility, and blood pressure (Thurmon, Tranquilli, and Benson, 1996). There are numerous benzodiazepine drugs on the market. They all have similar pharmacological profiles, but vary in potency and duration of effect, related to their affinity for the benzodiazepine receptor and their pharmacokinetic properties (Stoelting, 1999).

Flumazenil is a competitive benzodiazepine antagonist, and antagonizes the sedative and amnesic qualities of benzodiazepines (Stoelting, 1999). Minimal information exists on the use of these drugs specifically in primates. Information is extrapolated from their effects in people.

Diazepam Diazepam has been used with ketamine to immobilize olive baboons and suppress or eliminate the epileptoid movements characteristic of anesthesia with ketamine alone (Woolfson et al., 1980).

Midazolam Midazolam is approximately 2 times more potent than diazepam. Bioavailability after oral administration is approximately 50% (Paine et al., 1996; Thummel et al., 1996). In humans, its half-life is 1 to 4 hours.

Zolazepam Information on the clinical effects of zolazepam alone is limited. Plasma half-life is 1 hour in primates (Lin, 1996).

DRUG COMBINATIONS

It is common to combine two or more drugs to achieve immobilization of primates (Jalanka, 1989; Horne, 2001a). This is done to minimize volume, increase potency, achieve a stable safe plane of anesthesia with adequate muscle relaxation and analgesia, improve recovery, and minimize side effects. Combinations of different drugs or varying relative dosages of the same drug combinations may have different effects. Most combinations used in primate anesthesia include a dissociative anesthetic, and many use a reversible sedative, such as an α_2 -agonist or a benzodiazepine, to decrease the required dose of the dissociative drug. The drug combinations most commonly used for monkey anesthesia are reviewed in the following.

Tiletamine/Zolazepam

Tiletamine/zolazepam has been widely used in primates with minimal cardiopulmonary effects (Bree, 1972; Bree, Cohen, and Rowe, 1972; Horne, 2001). Dosages for

various species are not always based on well-controlled studies, but reflect subjective opinions from experienced investigators (Gray, Bush, and Beck, 1974; Schobert, 1987).

Wild black spider monkeys were anesthetized with dosages ranging from 11.6 to 18 mg/kg (Karesh et al., 1998), with the higher dosage resulting in more reliable and stable planes of anesthesia. Induction times were 2 to 4 minutes, with immobilization lasting from 80 to 150 minutes. Adult, free-living red howler monkeys were anesthetized with 22.5 mg/kg, and juveniles received 30.5 mg/kg. With these dosages, the induction period was 1 to 6 minutes, and immobilization varied from 40 to 300 minutes, with no apparent adverse effects (Agoramoorthy and Rudran, 1994).

Other researchers also describe the use of tiletamine/zolazepam for field anesthesia in various species with a good overall effect (Glander et al., 1991; Sleeman et al., 2000). For wild savanna baboons, 5 mg/kg is recommended as an anesthetic, with duration of approximately 1 hour. In cynomolgus macaques and vervet monkeys tiletamine/zolazepam (5 to 10 mg/kg IM) was adequate for ophthalmological surgery. These dosages produced a rapid onset and 30 to 50 minutes of surgical anesthesia, excellent muscle relaxation, absence of ocular movement, and a gradual emergence with no adverse effects (Kaufman and Hahnenberger, 1975).

For most species 2 to 5 mg/kg is effective for minor procedures, with small species requiring higher dosages than larger. In most, tiletamine/zolazepam induces a moderate tachycardia. In rhesus monkeys this combination induces little or no impairment of thermoregulation (Holmes and Hunter, 1980).

Tiletamine/zolazepam has a high therapeutic index, as reflected by the variety of published dosage recommendations. There are likely species differences, but the dosages probably reflect the different subjective opinions of investigators, since no dose titration studies are available. Recommended dosages for capture of free-living animals are high compared to those used in captive animals. A major advantage of this combination is high potency, which allows a small drug volume.

There are no reversal agents for tiletamine; and prolonged recovery periods are common. Hence, the investigator may have to spend time monitoring the recovery of immobilized wild animals that can not be abandoned in a sedated state. Including a reversible drug such as medetomidine to reduce the dosage of tiletamine/zolazepam has been used successfully in great apes (Horne et al., 1998). This combination probably could be used in all primate species but there are limited species-related dosage recommendations.

Ketamine/Diazepam

Immobilization of olive baboons with ketamine (10 mg/kg IM) and diazepam (0.20 to 0.36 mg/kg IM) was safe and efficient (Woolfson et al., 1980). This

combination was preferred for procedures requiring good muscle relaxation compared with ketamine alone (10 mg/kg).

DISSOCIATIVE ANESTHETIC/ α_2 -AGONIST

Ketamine/Xylazine

The combination of ketamine (5.25 mg/kg IM) with xylazine (0.45 mg/kg IM) enhanced analgesia, anesthesia, and muscle relaxation in rhesus macaques, compared with ketamine alone (Banknieder et al., 1978). Animals remained anesthetized for 44 minutes (range, 23–63 minutes). However, an important observation with this combination is that anesthetic emergence is fast. Animals were alert and standing only a few minutes after the anesthetic period. The presence of the pedal reflex preceded the end of the anesthetic immobilization by only 2 to 3 minutes. This duration coincides with ketamine redistribution and the quick recovery is probably a result of the arousability seen with α_2 -agonists.

In rhesus macaques the minimum effective dosage was 2.5 mg/kg ketamine with 0.25 mg/kg xylazine IM (Naccarato and Hunter, 1979). These investigators found a wide safety margin with this combination, but xylazine markedly reduced the thermoregulatory abilities of the animals. Yellow baboons receiving ketamine (11 mg/kg IM) and xylazine (0.5 mg/kg IM) were easily intubated, and anesthesia lasted from 90 to 125 minutes (White and Cummings, 1979). Recommendations for wild savanna baboons are ketamine (10 to 15 mg/kg IM) combined with xylazine (1 mg/kg IM) (Sapolsky and Share, 1998).

Ketamine/Medetomidine

Ketamine/medetomidine has been used in several primate species (Jalanka, 1989; Lewis, 1993; Horne et al., 1998; Vie et al., 1998). The combination has marked advantages over ketamine alone by reducing ketamine dosage, increasing sedation and muscle relaxation, and reducing sympathetic stimulation.

In cynomolgus monkeys there was little difference in the level of sedation, cardiovascular effects, anesthesia time, and recovery time between ketamine alone (10 mg/kg IM) or a combination of ketamine (2 mg/kg IM) and medetomidine (0.05 mg/kg IM). However, because of some unexpected quick recoveries, the investigators felt that this combination was unreliable and recommended caution in using it at these dosages.

Japanese macaques given ketamine (5 mg/kg IM) and medetomidine (0.05 mg/kg IM) had a mean induction time of 4 minutes and anesthetic duration of 65 minutes, with excellent muscle relaxation (Ølberg, 2004). After induction they had an initial heart rate of 100 bpm that slowly decreased to 60 bpm during anesthesia. The mean arterial pressure also decreased slowly from approximately 110 mmHg after induction to 70 mmHg

at the end. The respiratory rates were 40 breaths per minute throughout anesthesia. The animals were hypoxemic after induction, but maintained adequate oxygenation when breathing 100% oxygen through a face mask.

INHALATION ANESTHESIA

Inhalation anesthesia may be used alone or to maintain anesthesia after induction with injectable agents. The most commonly used inhalants, isoflurane and halothane, have a minimum alveolar concentration (MAC) in primates of 1.2% and 0.9%, respectively. The MAC of sevoflurane in primates is approximately 2% (Soma, Tierny, and Satoh, 1988). Small primates (i.e., tamarins and marmosets) can be manually restrained in a net and induced with an inhalant anesthetic through a face-mask or in an induction chamber. A clear advantage of inhalant anesthetics is that oxygen is used as carrier gas. This normally ensures adequate partial pressure of oxygen in the arterial blood during anesthesia.

ANALGESIA

Opioid agonists are powerful analgesic agents, but one should exercise care when using them in primates because of their strong ventilatory depressant effects. They should only be used if the animal is intubated and respiratory support can be given. Ketamine and medetomidine have strong analgesic properties, and are often used in the anesthetic protocol. Non-steroidal anti-inflammatory drug (NSAID) dosages are extrapolated from other species.

COMPLICATIONS

Catching and induction are two critical parts of primate anesthesia. There is a possibility for traumatic injury when using projectile darts. Furthermore, there is a possibility that the primate will fall down if sitting in a tree or on a shelf in the holding area. Nets might be used to catch a primate before it hits the ground. Once induction of anesthesia is achieved, complications are often related to the health state of the animal, drugs used, and the delivered dose of the respective drugs. Hypothermia is common and body temperature is monitored throughout the procedure.

Hypoxemia is caused by hypoventilation, pulmonary shunting, or ventilation-perfusion mismatch. The use of a pulse oximeter will help evaluate oxygen saturation throughout the procedure. Supplemental oxygen is administered through a face mask or endotracheal tube. Commonly used anesthetic agents such as ketamine (5 mg/kg IM) and medetomidine (0.05 mg/kg IM) may cause mild to severe hypoxemia if the animals are breathing room air shortly after induction (Ølberg,

2004). The use of reversible anesthetic agents adds safety to the procedure. A laryngoscope and suitable endotracheal tube always should be available during anesthesia, as well as equipment necessary to give IV fluid.

RECOVERY

Recovery is performed in a quiet, confined space that prevents climbing and allows constant monitoring. A towel or other insulating material minimizes heat loss to the floor. The primate is not reunited with its troupe until it has fully recovered.

SUGGESTED PROTOCOLS

In this author's experience medetomidine/ketamine works well for injectable anesthesia of most species.



Figure 32.3. Small primates such as this squirrel monkey, or larger animals immobilized with parenteral anesthetics, can be masked induced with an inhalant anesthetic.



Figure 32.4. Small primates can be induced in induction boxes with an inhalant anesthetic administered in oxygen.

Animals weighing less than or equal to 1 kg are anesthetized with 0.05 mg/kg medetomidine and 10 mg/kg ketamine IM. Animals weighing greater than a few kilograms can be anesthetized with 5 mg/kg ketamine and 0.05 mg/kg medetomidine IM. Most primates sleep with this combination for approximately 45 to 60 minutes, but recover quickly. Anesthesia can be maintained with isoflurane in oxygen for a longer duration. For procedures longer than 60 minutes this author recommends tiletamine/zolazepam if inhalation anesthesia is not an option. Inhalation anesthesia works well alone for species that are easy to manually restrain, and is excellent for maintenance once induction is achieved (Figures 32.3 and 32.4).

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33 Great Apes Jonathan Sleeman

INTRODUCTION

Anesthesia of great apes can be challenging owing to their relatively large size, physical strength, agility, and intelligence. In particular, great apes can be very sensitive to changes in their normal environment. Even very subtle perturbations can cause apes to become excited or aggressive, such that anesthetic induction can be very distressing to both animal and anesthesiologist. However, there are sizeable populations of great apes in zoological collections and research institutions because of their endangered status, and use as animal models for human diseases, respectively. Consequently, anesthesia is frequently performed on these species, which has resulted in the development of a body of knowledge. However, captive apes often suffer from medical conditions such as cardiomyopathy that can complicate anesthetic events. Recent studies have focused on orally administered, transmucosally absorbed, anesthetic agents as alternative, less stressful, methods of anesthetic induction. Finally, there is increasing conservation management of in situ great ape populations, which has resulted in the development of field anesthesia techniques for freeliving great apes for the purposes of translocation, reintroduction into the wild, and clinical interventions.

TAXONOMY, BIOLOGY, AND MEDICAL CONDITIONS RELATED TO ANESTHESIA

Great apes include the bonobo (*Pan paniscus*), four subspecies of chimpanzees (*Pan troglodytes*), two species of gorillas (*Gorilla gorilla*, and *Gorilla beringei*) each with two subspecies, and two subspecies of orangutans (*Pongo pygmaeus*). They are all tropical Old World species, and all are considered endangered.

Bonobos are the smallest of the great apes, with an adult weight range of 25 to 45 kg. Chimpanzees usually weigh 40 to 90 kg, orangutans weigh 40 to 189 kg, and gorillas are the largest with an adult weight range of 70

to 340 kg. Males are larger for all species. All are social, with complex social structures and behaviors, except for orangutans, which are solitary. Great apes have a close taxonomic relationship with humans. Consequently, there are many anatomical similarities; thus, human anesthetic equipment such as face masks is often used in preference to veterinary equipment. In addition, there is a high potential for pathogen exchange between humans and great apes, necessitating appropriate disease preventive measures.

Their large size, agility and physical strength, as well as large teeth and strong jaws, create the potential for human injury during anesthetic procedures. For this reason, physical restraint and sedation of apes is generally not practical, and most procedures require the animal to be at least stage III of anesthesia. Human safety is of paramount importance during any anesthetic event involving great apes, and it is important to have an experienced, well-trained team of individuals. Because of the zoonotic disease concerns mentioned in the preceding, all persons in close proximity to apes must wear personal protective equipment such as face masks and latex gloves. It would also be prudent to establish escape and bite wound protocols as well as have access to a bite wound kit for first aid treatment of persons who may be bitten.

Unique respiratory anatomical features include laryngeal air sacs in all great apes, which are more extensive in gorillas and orangutans. These air sacs are prone to bacterial and yeast infections (Janssen, 1993). Laryngeal air sacculitis could complicate general anesthesia due to the risk for fatal pneumonia from the aspiration of purulent material. Apes with air sacculitis should be intubated with cuffed endotracheal tubes, and the condition should be treated prior to any elective anesthesia. In addition, great apes have relatively short tracheas, and care must be taken to ensure that a primary bronchus is not inadvertently intubated (Loomis, 2003).

Cardiovascular diseases are a significant cause of morbidity of captive great apes. Fibrosing cardiomyopathy

and aortic dissection are particularly common in older male gorillas. Other cardiac conditions include, for example, congestive heart failure, coronary atherosclerosis, and hypertension (Loomis, 2003). All of these conditions could complicate anesthesia or result in anesthetic death. Older apes as well as animals with a history of cardiovascular disease should be carefully evaluated prior to anesthesia, and carefully monitored during the procedure. Consultation with human anesthesiologists experienced with these medical conditions in human patients may be beneficial.

Captive apes are also prone to obesity. This may have been a contributing factor in the development of fatal acute respiratory distress syndrome owing to negative pressure pulmonary edema in an orangutan under Telazol-induced anesthesia (Kenny et al., 2003). The authors speculated that an acute upper airway obstruction may have been the precipitating factor. Orangutans have a propensity for laryngospasm during anesthesia. In addition, a thick robust tongue, a long flaccid soft palate, and excessive caudal pharyngeal tissue may predispose this species to this syndrome during anesthesia. Obesity and respiratory disease could also compromise respiratory function in poorly positioned patients during anesthesia. Kenny et al. (2003) recommended that orangutans should be properly positioned with a patent airway during anesthetic induction, as well as the use of thick-walled, armored, or re-inforced endotracheal tubes with a stylet to facilitate rapid intubation.

Some Old World nonhuman primates in estrus develop large genital tumescence. This swelling of the sexual skin can be quite prominent in chimpanzees, and is very vascular and friable. Care must be taken to avoid darting this area as severe hemorrhage may result (Fowler, 1995).

Venous access can be accomplished at several sites. The femoral vein at the femoral triangle is readily available. In addition, the saphenous vein on the posterior surface of the lower leg, as well as the cephalic vein are usually visible, especially in larger animals. Hendrix (2006) reports the use of the dorsal pedal artery as a site for direct blood pressure measurement and blood-gas sampling in an orangutan. The author has also used the femoral artery for the same purpose in a chimpanzee.

ANESTHETIC PROTOCOLS

Induction

As with any species, a pre-anesthetic assessment is vital. However, this can be challenging in great apes and significant diseases may go unrecognized. Furthermore, estimated body weights are often inaccurate, and one study reported that even experienced personnel overestimated the weights of chimpanzees by as much as 28% (Adams et al., 2003).

Great apes should be fasted and water withheld for 12 to 24 hours prior to anesthesia. However, this is often

a clue that a procedure is imminent and will result in increased agitation, vocalization, and aggression. Consequently, it is important to keep the environment as stress-free and close to the normal routine as possible to avoid this distress. In addition, some individuals practice pica or coprophagy as a result of fasting (Loomis, 2003). Furthermore, apes can remember and recognize individual persons, and the presence of the veterinarian often induces a violent response. Operant conditioning can train some individuals to present a muscle mass for hand injection of anesthetic agents. Otherwise, the agents are usually delivered in lightweight darts propelled by remote delivery systems such as blow pipes or muzzle velocity adjustable dart guns. The least traumatic remote delivery system should be used to prevent injury. All attempts should be made to dart the animal without warning, as once alerted the individual or group will become agitated and mobile, making darting very difficult. Protective clothing, including face shields, may be necessary as chimpanzees have a propensity to spit water, throw fecal matter, and other material with surprising accuracy, as well as returning darts with some force. In addition, apes have surprisingly long limbs and grab at loose clothing, glasses, and even the dart gun. Ideally, potent drugs that require a small volume for injection should be used as apes can remove a dart very quickly prior to full injection of the drug.

Darting individuals housed in a social group can be particularly challenging and isolation of the targeted individual from the group prior to anesthesia may not be possible, or could be very stressful. Once alerted to the event the whole group may act aggressively toward humans in close proximity, which can be very intimidating. However, it is important to have a mechanism to isolate and retrieve the anesthetized individual, especially in the event of an anesthetic emergency. Appropriate facilities that allow shifting of animals, and securing areas or rooms is very helpful. Removal of enclosure furniture prior to darting may be beneficial as apes can be very adept at hiding, or adopting body positions, to avoid the dart.

Induction Agents

Injectable induction agents and dosages commonly used alone or in combination are listed in Table 33.1. The protocols described in this section pertain to captive great apes unless otherwise noted.

Ketamine Hydrochloride Ketamine hydrochloride alone has been used successfully in chimpanzees, gorillas, and orangutans with smooth and rapid induction (3–10 minutes) using standard intramuscular dosages in Table 33.1 (April, Tabor, and Gerety, 1987; Raphael et al., 2001). These studies reported adequate muscle relaxation, good analgesia, and minimal cardiopulmonary changes. Recovery occurred within 40 to 60 minutes

Table 33.1. Range of dosages of injectable anesthetic induction and reversal agents used in great apes.

Drug	Chimpanzee	Gorilla	Orangutan	References
Induction Agents				
Ketamine	5-20	6-10	6-10	3, 25, 30, 31, 33
Ketamine/xylazine	10-20/1		5-7/1-1.4	2, 3, 22, 23, 25
Ketamine/medetomidine	2-5/.0205	2-5/.0205	Use reported	12, 13, 14, 16, 26
Ketamine/midazolam		9/0.05	1-2/0.03	11, 27
Telazol	2-6	2-6	2-6.9	8, 23, 25, 27, 31
Telazol/medetomidine	1.25/0.03-0.04		0.8-2.3/0.02-0.06	6, 7, 12, 13, 14
Reversal Agents				
Atipamezole	0.1-0.5 (intramuscular/	(all species)		
•	intravenous)			13, 16, 28
Yohimbine	0.125-0.25	(all species)		28
Flumazenil	0.02–0.1 (intravenous)	(all species)		28
Naloxone	0.02 (intramuscular/intravenous)	(all species)		28

Dosages are listed as mg/kg for intramuscular injection unless stated.

and all individuals were calm with minimal anxiety and ataxia. However, ketamine is irreversible, has a short duration of action with sudden unexpected recoveries, and tolerance develops with repeated use (April, Tabor, and Gerety, 1982; Lewis, 1993). Conversely, incremental doses of ketamine to prolong anesthesia can result in an extended recovery time of several hours. Ketamine does maintain laryngeal reflexes to some extent, but this does not obviate the need for careful airway management. It can also induce hypersalivation, which can be prevented or controlled using an anticholinergic agent.

Ketamine and Xylazine The disadvantages of ketamine resulted in the development of protocols combining ketamine with α_2 -agonists. April, Tabor, and Gerety (1987) reported the use of a combination of ketamine and xylazine in chimpanzees delivered intramuscularly that resulted in similar induction time compared to ketamine alone, but with a greater depth of anesthesia characterized by greater muscle relaxation and analgesia, as well as cardiopulmonary stability, and longer but uneventful recoveries.

Ketamine and Medetomidine Lewis (1993), Horne, Norton, and Loomis (1997), and Adams et al. (2003) have also investigated the use of ketamine in combination with medetomidine delivered intramuscularly by remote injection. Use of medetomidine reduced the required dose of ketamine at least fivefold. This combination provided a rapid and safe method of anesthetic induction, with complete immobilization achieved within 3 to 15 minutes for both chimpanzees and gorillas (Horne, Norton, and Loomis, 1997; Adams et al., 2003). Horne, Norton, and Loomis (1997) reported that it was very important for the animal be left undisturbed for the initial 10 minutes after administration as attempts to manipulate or move it prior to this resulted in rapid arousal. Cardiovascular effects appeared to be minimal; the only noteworthy change was a modest increase in

blood pressure soon after induction (Horne, Norton, and Loomis, 1997). However, intravenous administration of medetomidine may induce a transient bradycardia (Horne, 2001). Reversal with atipamezole, at five times the dose of medetomidine, was rapid, smooth, and complete within 10 to 13 minutes after intramuscular injection and within 6 minutes for intravenous administration with no evidence of resedation or residual effects. This combination also provided a smooth transition to inhalation anesthesia. Recoveries can be quite sudden, even without use of the reversal agent (Sleeman, personal observation), which could create a dangerous situation for the unprepared anesthesiologist.

Telazol and Telazol Combinations Telazol is a 1:1 combination of tiletamine, a cyclohexamine, and zolazepam, a benzodiazepine and has been used widely in primates with published dosages for chimpanzees, gorillas, and orangutans (Table 33.1). In addition, Telazol has been used in combination with medetomidine for chimpanzees (Horne et al., 1998) and free-ranging orangutans (Fahlman, Bosi, and Nyman, 1999, 2006; see Field Anesthesia section below). In all these studies, Telazol alone, or in combination with, an α₂-agonist produced smooth rapid induction within 1 to 7 minutes and with stable cardiopulmonary parameters, although significantly lower blood pressures were observed in chimpanzees induced with Telazol/medetomidine and maintained with isoflurane, compared with animals anesthetized with ketamine/medetomidine and isoflurane (Horne et al., 1998). Furthermore, recoveries from Telazol/medetomidine anesthesia in chimpanzees were prolonged (1-5 hours) and were characterized by signs of extreme drowsiness, dizziness, ataxia, and adverse gastrointestinal effects such as vomiting. Flumazenil transiently increased alertness in chimpanzees but did not significantly enhance the speed or quality of recovery (Horne et al., 1998). A similar effect after administration of flumazenil to gorillas has been noted (Sleeman et al., 2000). Fowler (1995) noted that the recovery time for Telazol alone is dose dependent and recommended the use of low doses for quick procedures (Fowler, 1995).

Other Combinations Loomis (2003) also lists the use of various other combinations in great apes including ketamine (1 mg/kg)/xylazine (0.25 mg/kg)/Telazol (1.25 mg/kg) as well ketamine (2–3 mg/kg)/medetomidine (20–40 μ g/kg)/butorphanol (0.2–0.4 mg/kg) and ketamine (3 mg/kg)/butorphanol (0.4 mg/kg)/midazolam (0.3 mg/kg), although no details were given. Hanley et al. (2006) also reported the use of a combination of ketamine (5.66 mg/kg) and Telazol (3.4 mg/kg) delivered intramuscularly to induce anesthesia in an orangutan.

ORAL ADMINISTRATION OF TRANQUILIZERS AND ANESTHETICS

Because of the stress of remote delivery injection of anesthetic agents, recent studies have focused on oral delivery and/or transmucosal absorption of preanesthetic and anesthetic agents. The techniques described can have variable and unpredictable results, but are a useful alternative method of delivery to consider. Despite the introduction of liquid or food material into the oral cavity immediately before anesthetic induction and increasing the potential for aspiration, such complications have not been reported. Use of metoclopramide (0.4 mg/kg) orally to prevent emesis prior to orally administered anesthetic agents has been described (Miller et al., 2000).

Neuroleptic Agents

For anxiolytic effects, the neuroleptic drug zuclopenthixol at dosages of 0.1 to 0.36 mg/kg by mouth twice daily was used in gorillas undergoing a prolonged journey (Vogelnest, 2001). These animals were calm, traveled well, and maintained good appetites during their transportation.

Benzodiazepines

Benzodiazepines have minimal effects on cardiopulmonary function and are considered safe to use in primates (Horne, 2001). Diazepam can be given orally as a pre-anesthetic agent and may provide some degree of sedation prior to anesthetic induction. Raphael et al. (2000) reported administering 5 mg diazepam orally to juvenile gorillas prior to anesthetic induction. In addition, Miller et al. (2000) described the use of diazepam for its sedative effect at 0.2 mg/kg given orally 90 to 120 minutes prior to anesthetic induction.

Cyclohexamines and α_2 -Agonists

Orally administered detomidine (0.32 mg/kg) and ketamine (9.6 mg/kg) was used to successfully sedate gorillas

prior to remote delivery of Telazol at a dosage of 0.94 mg/kg (Miller et al., 2000). The drugs were administered by keeper staff using husbandry training techniques. Lateral recumbency was achieved at 17 minutes in one animal that received a full dose. For the other animals that received partial doses, the first signs of sedation were seen around 15 minutes. In all cases, the gorillas had only mild responses to darting and were subjectively judged to be less stressed than darting alone based on decreased screaming, charging, and other stress behaviors.

Medetomidine transmucosally administered at 50 to $100\,\mu\text{g/kg}$ prior to immobilization with ketamine by injection resulted in variable effects (Kearns, Afema, and Duncan, 1998). Some animals that had not had previous immobilization experience were noticeably sedated, whereas other more experienced chimpanzees showed little or no sedation. Consequently, medetomidine appears to be a useful premedicant only in chimpanzees that are not stressed or agitated prior to drug administration.

Telazol delivered orally at a dosage of 16 mg/kg, administered in about 30 ml of Coca-Cola was used to successfully immobilize a chimpanzee (Knottenbelt and Knottenbelt, 1990). Lateral recumbency was achieved within 7 minutes with no response to external stimuli. Cardiopulmonary function was considered stable, and both pharyngeal and laryngeal reflexes were present. The chimpanzee began to respond to external stimuli after 40 minutes, and recovery was uneventful.

Opioids and Opioid Combinations

Preliminary trials with orally delivered, transmucosally absorbed carfentanil citrate alone at dosages of 2 to 4 μg/kg in chimpanzees provided nearly or complete immobilization after 22 minutes, but were accompanied by severe respiratory depression, including one case of respiratory arrest and death (Kearns, Swenson, and Ramsay, 1999). Consequently, administration of transmucosal carfentanil alone for immobilization of chimpanzees is not recommended. However, the administration of oral droperidol at a dose of 1.25 mg for juvenile chimpanzees and 2.5 mg for adults chimpanzees and bonobos 45 minutes prior to transmucosal carfentanil administration at 2.0 µg/kg provided an effective premedication regimen that produced profound sedation prior to the intramuscular delivery of Telazol (3 mg/kg) for anesthetic induction (Kearns, Swenson, and Ramsay, 2000). Carfentanil was administered by enticing the animal to the front of the cage and expelling the drug from a 0.5-ml syringe directly onto the oral mucosa, or by mixing the drug with honey or marshmallow crème. Kearns, Swenson, and Ramsay (1999, 2000) noted that chimpanzees showed reluctance to accept the drug. This combination provided smooth induction and heavy sedation or light anesthesia approximately 25 minutes after carfentanil administration. At that time naltrexone and Telazol were

combined into one intramuscular injection for anesthetic induction delivered by hand or remote injection. Naltrexone was administered at 100 times the carfentanil dose in milligrams. The primary side effect noted was respiratory depression, but was adequately managed by administration of the narcotic antagonist at the time of anesthetic induction with Telazol. However, the authors also recommended providing supplemental oxygen as well as preparing a naltrexone dart in advance as a precaution. In addition, a side effect of facial pruritus was noted in some individuals.

Transmucosal fentanyl formulations approved for human use have also been used in great apes. Hunter et al. (2004) trained animals to accept, after an overnight fast, a placebo candy lollipop and to suck on in slowly. After 4 to 6 weeks of training, the apes were then offered the fentanyl lollipop at an intended dose of 10 to 15 ug/kg. Orangutans and gorillas accepted the treated lollipops and displayed signs of adequate sedation in 30 to 45 minutes, and responded minimally to darting. However, the chimpanzees refused the fentanyl lollipops and were suboptimally sedated with unpredictable results. The resulting plasma concentrations of fentanyl supported transmucosal absorption in orangutans and gorillas; however, none of the chimpanzees had detectable concentrations of norfentanyl in their plasma. Success of this technique was dependent on an effective training program, cooperation of the keeper staff, and adequate housing facilities.

ANESTHETIC MAINTENANCE AND MONITORING

For prolonged procedures, intubation and maintenance of anesthesia using inhalation agents delivered in oxygen is recommended. For most of the induction agents mentioned in the preceding, the plane of anesthesia may not be adequate to allow intubation, and it may be necessary to deliver inhalation agents to the animal using a tightly fitting human face mask prior to intubation. Great apes are best intubated in dorsal recumbency with the head extended off the edge of the table. Pulling the tongue forward may help to visualize the larynx. The base of the tongue should then be depressed using a Macintosh laryngoscope blade. Great apes are prone to hypersalivation and laryngospasm, especially under ketamine anesthesia (Horne, 2001). Applying lidocaine to the glottis several minutes before intubation will help to prevent this (Horne, 2001; Adams et al., 2003). Great apes require cuffed Murphy tubes ranging in size from 6 to 12 mm. As mentioned, the short tracheas predispose to intubation of a primary bronchus; thus, once the tube is in place both sides of the chest should be monitored for air sounds.

Isoflurane is commonly used to prolong and maintain anesthesia in great apes (Cook and Clarke, 1985; Horne, Norton, and Loomis, 1997; Horne et al., 1998;

Adams et al., 2003; Hendrix, 2006); however, it has potent vasodilatory properties that can cause severe hypotension (Horne, 2001). In addition, as most animals will have received an anesthetic induction agent, the minimum alveolar concentration (MAC) of isoflurane must be reduced accordingly. For example, chimpanzees and gorillas induced with medetomidine and ketamine required masking with 2% to 3% isoflurane in 100% oxygen to permit intubation followed by 0.5% to 1.5% isoflurane for anesthetic maintenance using a non-rebreathing circuit (Horne, Norton, and Loomis, 1997). Blood pressure, heart rate, hemoglobin saturation, and end-tidal CO₂ remained within normal limits using this regimen. Animals induced with medetomidine and Telazol required a lower MAC and could be maintained on a mean level of 0.8% isoflurane in 100% oxygen (Horne et al., 1998). In addition, the latter anesthetic induction combination appeared to potentiate the vasodilatory effects of isoflurane placing the animals at risk for hypotension, requiring close monitoring of blood pressure. Sevoflurane has been used experimentally in nonhuman primates and may be useful in great ape anesthesia (Horne, 2001).

Injectable agents have also been used to maintain anesthesia in great apes. Fentanyl ($10\,\mu g/kg$), midazolam ($0.4\,mg/kg$) and vecuronium ($0.1\,mg/kg$) were delivered intravenously as part of a balanced anesthesia for a juvenile orangutan undergoing heart surgery. Ketamine infusion ($50\,\mu g/kg$ per minute) and low dose isoflurane between 0.2% to 1%, in a 1:1 air:oxygen mixture was used to maintain anesthesia in this patient (Greenberg et al., 1999). Historically, supplemental doses of ketamine have been used to prolong anesthesia, but result in a prolonged recovery (Lewis, 1993).

Hendrix (2006) reported the use of thiopental (2.1 mg/kg intravenously) to allow intubation after anesthestic induction with intramuscular ketamine (1 mg/kg) and midazolam (0.03 mg/kg) in an orangutan undergoing laparoscopic tubal ligation. After intubation, the animal was maintained on 1.5% to 2.25% isoflurane delivered in 100% oxygen at 1.5 L per minute via a circle breathing system. Intermittent positive pressure ventilation at a rate of 10 to 20 breaths per minute, 800-ml tidal volume, and a peak inspiratory pressure of 20 cm water was used to overcome the respiratory compromise induced by the head down (Trendelenburg) position and abdominal insufflation. Hypertension (highest mean arterial blood pressure was 158 mmHg) was also noted and was thought to also be caused by the insufflation or use of ketamine. Increasing the inhalant concentration improved the animal's relaxation and resolved the hypertension.

Use of propofol to maintain anesthesia has been reported in orangutans at 50 mg/kg (total dose) intravenously (Kenny et al., 2003), and 0.19 mg/kg per minute intravenously in combination with intermittent supplemental boluses of ketamine (Hanley et al., 2006),

as well as a gorilla (dose not reported; Raphael et al., 2001). Kenny et al. (2003) reported unsatisfactory results.

Use of adjuncts such as atropine sulfate at 2 to 5 mg as a single injection for juvenile chimpanzees (April, Tabor, and Gerety, 1987), 0.04 mg/kg intramuscularly for gorillas (Raphael et al., 2001), 0.01 mg/kg intramuscularly for an orangutan (Hendrix, 2006) and glycopyrrolate at 0.01 mg/kg (Greenberg et al., 1999) intramuscularly also for an orangutan has also been reported, presumably to control hypersalivation and/or bradycardia.

Careful and close anesthetic monitoring is warranted for great apes, whenever possible. Simultaneous and continuous monitoring of oxygen hemoglobin saturation (pulse oximetry), end-tidal CO_2 (capnography), blood pressure (oscillometry), cardiac electrical activity (ECG) is most important (Horne, 2001) (Figure 33.1).

Significant increases in blood pressure with increasing age have been reported in chimpanzees, necessitating closer monitoring in older individuals to detect possible hypertension (Eichberg and Shade, 1987). Frequent analysis of arterial blood gases can also be very useful. Published cardiopulmonary parameters for great apes under various anesthetic regimens are summarized in Table 33.2. Hendrix (2006) also reports arterial bloodgas and end-tidal $\rm CO_2$ values for an orangutan undergoing a laparoscopic procedure.



Figure 33.1. Gorilla undergoing a magnetic resonance imaging scan. Note the electrocardiography and pulse oximetry probe on the tongue. Close anesthetic monitoring of great apes, whenever possible, is very important. (Photo taken by Julie Wilson, Oakridge Veterinary Imaging.)

ANESTHETIC RECOVERY

Injectable reversal agents and dosages commonly used are listed in Table 33.1. As noted, once reversed, recovery can be quite sudden. Consequently, except for emergency situations, these agents should only be administered once the animal is safely secured. The immobilized animal should be allowed to recover in isolation to prevent attack from other members of the group. If the procedure has lasted for only a few hours, then return to the group should be uneventful. If an animal must be separated for longer periods then behavioral problems may ensue with reintroduction (Fowler, 1995).

FIELD ANESTHESIA

There is increasing conservation management of *in situ* great ape populations, which has resulted in the development of field anesthesia techniques for free-living great apes for the purposes of translocation, reintroduction into the wild, and clinical interventions. Anesthesia of great apes under field conditions is inherently riskier for the animals and humans conducting the procedure owing to more variables and less control over the animal.

Sleeman et al. (2000) summarized the field anesthesia of 24 free-living human-habituated mountain gorillas (Gorilla beringei beringei) using either ketamine (dosage 7 mg/kg) or Telazol (dose range 90-325 mg) delivered by remote injection. Anesthesia was mostly performed to facilitate medical treatment. Induction time for both agents was approximately 5 minutes, and recovery was significantly shorter for ketamine (mean = 42 minutes) compared with Telazol (mean = 75 minutes). The authors concluded that anesthesia could be safely performed, even among a large group of gorillas, although the procedures frequently required the entire day. Success of the procedures were dependent the assistance of local field staff who had extensive knowledge of gorilla behavior as well as the landscape. Other key factors included darting the animals without warning; keeping the other gorillas away from the anesthetized animal by creating a visual barrier; remaining with the gorilla until it was fully recovered and able to rejoin its group; and reassuring the patient during recovery by grooming the animal and mimicking gorilla vocalizations. Neither drug appeared to produce novel physiological effects, although some

Table 33.2. Range of physiological parameters reported in great apes under various anesthetic regimens.

Physiological Parameter	Chimpanzee	Gorilla	Orangutan	References
Heart rate (Beats per minute) Respiratory rate (Breaths per minute)	60–200	44-144	64-114	7, 12, 13, 14, 31
	20–60	14-41	24-120	7, 20, 31
Body temperature, °C	36.8 (mean)	35.4–40.0	34.7–38.6	7, 20, 31
Mean arterial blood pressure, mmHg	73–215	73–121	71–148*	5, 7, 12, 13, 14

^{*}Systolic blood pressure (mmHg)



Figure 33.2. Field anesthesia of a mountain gorilla (Gorilla beringei). It is important to wear personal protective equipment such as face masks and latex gloves to prevent possible pathogen exchange. Note the visual barrier to keep the other gorillas away from the anesthetized animal. (Copyright Jonathan Sleeman.)

gorillas had low hemoglobin oxygen saturation values (range = 86%–88%). The authors reported that the relatively high altitude at which the procedures were performed may have contributed to the apparent hypoxemia, and consequently recommended providing supplemental oxygen.

Habitat destruction and fragmentation results in scattered and isolated populations of orangutans, and translocation of isolated individuals to protected habitat is an important, albeit somewhat controversial, conservation strategy (Andau, Hiong, and Sale, 1994; Kilbourn et al., 1997, 2003). The use of various anesthetic protocols to assist with orangutan translocations have been described including Telazol (3-6.9 mg/kg; Andau, Hiong, and Sale, 1994; Kilbourn et al., 1997, 2003), combined ketamine (5-7 mg) and xylazine (1-1.4 mg/kg) (Andau, Hiong, and Sale, 1994; Kilbourn et al., 1997, 2003) as well as medetomidine (0.018–0.025 mg/kg) combined with Telazol (0.9–1.3 mg/kg) (Fahlman, Bosi, and Nyman, 1999, 2006). Kilbourn et al. (1997) recommended Telazol because of shorter induction times and smaller dart volume. However, Andau, Hiong, and Sale (1994) advised the use of ketamine/xylazine where rapid recovery is desired owing to the availability of the xylazine reversal agent, yohimbine hydrochloride. The induction time for both Telazol and ketamine/xylazine was 4 to 5 minutes; however, if additional doses were required, then induction time increased to 16.67 minutes (Andau, Hiong, and Sale, 1994). Recovery times were around 42 minutes for ketamine/xylazine and slightly longer for Telazol.

In typical translocation operations, the orangutan was darted approximately 15 meters up a tree. Both Telinject and Distinject systems were used along with 1 or 3 ml plastic or metal darts with 19- to 20-mm

needles with retaining collars. The animals were allowed to fall naturally to the ground; the tangle of vines providing natural cushioning, or nets were used to catch the animal. Andau, Hiong, and Sale (1994) reported no mechanical injuries from the capture, handling, and transport of animals, although the authors cautioned against darting animals at a height of over 30 meters. Two fatalities were recorded by Andau, Hiong, and Sale (1994). One was caused by hyperthermia as a result of an immobilized animal remaining high in the nest fully exposed to the sun, and the other was a nursing infant that accidentally received the dart intended for its mother. The authors concluded that both Telazol and ketamine/xylazine provided satisfactory immobilization to facilitate the capture and translocation of orangutans, although the need to provide additional doses of drug in several animals suggested that a somewhat higher initial dose may be appropriate.

The medetomidine/Telazol combination delivered intramuscularly to semi-captive or free-ranging orangutans provided rapid smooth induction with recumbency within 1 to 7 minutes (Fahlman, Bosi, and Nyman, 1999, 2006). It was considered favorable for remote drug delivery to free-ranging orangutans when compared with Telazol alone owing to low drug volume and more controlled descent from the trees. This combination resulted in the animals being able to grip branches during the descent down the tree, making the fall more gradual with less risk for injury. This is in contrast with Telazol alone in which the animals rapidly became immobilized and fell unconscious from the tree. Adequate anesthetic depth with good muscle relaxation was also reported. Heart and respiratory rates and hemoglobin oxygen saturation remained stable, although occasional measurements were below 90%; however, significant declines in systolic blood pressure (below 80 mmHg in some cases) and body temperature were recorded. The authors recommended using intravenous fluids and oxygen supplementation to prevent these side effects. One orangutan developed hyperthermia and apnea during translocation, but was successfully resuscitated. The authors reported that additional doses of Telazol were required during the orangutan translocations, and recommended further studies to determine optimal dosages of this combination in free-ranging orangutans. Atipamezole was administered intramuscularly at five times the dosage of medetomidine 23 to 54 minutes after injection of medetomidine/Telazol, or the last additional dose of Telazol, and first signs of recovery from anesthesia were noted on average approximately 10 minutes (range 3-27 minutes) after injection. The recoveries were reported to be smooth and calm.

Returning confiscated and orphaned chimpanzees to native habitat is also an increasingly considered as well as controversial conservation strategy. Tutin et al. (2001) described the successful release of 20 wild-born chimpanzees, and the use of anesthesia to facilitate this

project. Capture of chimpanzees prior to release was performed by administering an anesthetic either by hand or remote injection. In addition, chimpanzees were maintained under anesthesia during the boat journey to the release site in order to minimize stress. Although details of the anesthetic protocols used were not given, having an experienced team to decrease the risks of drowning as chimpanzees were often in trees overhanging a lagoon, as well as controlling aggression to humans was recommended.

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Canids

R. Scott Larsen and Terry J. Kreeger

TAXONOMY AND BIOLOGY RELATED TO ANESTHESIA AND HANDLING

The 36 species of non-domestic canids currently recognized by the World Conservation Union Canid Specialist Group (Sillero-Zubiri et al., 2004) are listed in Table 34.1.

Many canids are pack animals. Reintroduction after prolonged separation (more than 12 hours) may result in extensive fighting, so animals should be kept with the pack as much as possible. Even if it is necessary to perform frequent immobilizations on an individual, it is generally preferable to perform procedures as quickly as possible and return the animal to the pack each time, rather than separating the animal and then attempting reintroduction (Kreeger, 1992).

Most canids are fast, elusive, and cunning, making them challenging to successfully immobilize in the wild. Some are also nocturnal. Jackals have extremely fast reaction times to sound and can move out of the path of slow-moving darts (McKenzie and Burroughs, 1993).

ANATOMY AND PHYSIOLOGY RELATED TO ANESTHESIA

The anatomy and physiology of non-domestic canids are similar to those of domestic dogs and do not warrant extensive review. The panting mechanism is important in evaporative cooling and thermoregulation. Lateral nasal glands supply moisture needed for evaporation, and heat is dissipated as the animal breathes in through the nose and out through the mouth (Kennedy-Stoskopf, 2003). This panting mechanism may be compromised during anesthesia, so careful attention to body temperature is warranted, especially if the mouth is held closed. Body temperature may become markedly elevated during restraint, so other methods must be used to prevent severe persistent hyperthermia if the animal cannot pant.

A few canids go through seasonal torpor or hibernation. Raccoon dogs hibernate during the coldest winter periods. At these times they have increased fat deposits and lower basal metabolic rates, as well as lower cortisol, thyroid, and insulin levels (Asikainen et al., 2004), all of which may influence the species' response to anesthetic drugs.

ANALGESIA

It can probably be assumed that local anesthetics, nonsteroidal anti-inflammatory drugs, and opioid analgesics that are acceptable for domestic dogs are also acceptable for non-domestic canids at similar dosages. Analgesics reported for non-domestic canid species are listed in Table 34.2.

RELEVANT PHYSICAL RESTRAINT TECHNIQUES

Canids are strong, fast, and agile. Their teeth are large and sharp, their jaw muscles are strong, and most canids can bite through heavy leather gloves. Gloves may be worn to handle canids; not to protect the handler from bite injuries, but to protect against scratches from the nails. However, gloves may restrict hand agility and decrease grip control, so some handlers prefer not to use gloves.

Many non-invasive procedures can be performed without anesthesia in smaller species such as foxes (Brash, 2003). Canids can be caught and temporarily restrained in large fishing nets, but substantial proficiency is needed to safely restrain large canids this way. Once in the net, animals can be pinned behind the head using a soft broom, forked stick, net, or catch pole. Canids should be pinned while injections are made (Kreeger, 1992). A towel or cloth should be placed over the eyes to decrease visual stimulation, calm the animal, decrease stress, and speed induction for chemical sedation and immobilization.

Table 34.1. Taxonomic and biologic information for canids.

				Adult Body Wt (kg)		Longevity (yr)
Genus	Species	Common Name	Female	Male	Combined	Captive [Wild]
Alopex	lagopus	Arctic fox	2.4-4.8	2.7-5.4		11
Atelocynus	microtis	Short-eared dog			9-10	9-11
Canis	adustus	Side-striped jackal	7–10	7–12		10-12
	aureus	Golden jackal	6.5-7.8	7.6-9.8		14
	latrans	Coyote	7.7-15	7.8-15		21 [16]
	lupus	Grey wolf			$23-60^{a}$	16 [13]
	lupus dingo	Dingo	8-17	7–22		13 [7-8]
	mesomelas	Black-backed jackal	6-10	6-12		[10-12]
	rufus	Red wolf	20-30	22-34		[13]
	simiensis	Ethiopian wolf	11-14	14-19		[12]
Cerdocyon	thous	Crab-eating fox			4.5-8.5	[9.2]
Chrysocyon	brachyurus	Maned wolf			21-30	16
Cuon	alpinus	Dhole	10-13	15-20		16 [7-8]
Lycaon	pictus	African hunting dog	19-27	25-35		[11]
Nyctereutes	procyonoides	Raccoon dog	3-13	3-12		13
Otocyon	megalotis	Bat-eared fox	3.2-5.4	3.4-4.9		13
Pseudalopex	culpaeus	Culpeo (Andean fox)	4-10	3.4-14		[11]
•	fulvipes	Darwin's fox	1.8-3.7	1.9-4.0		[7]
	griseus	Chilla	2.5-5	3.1-4.9		5
	gymnocercus	Pampas fox	3.0-5.7	4.0-8.0		14
	sechurae	Sechuran fox			2.6-4.2	
	vetulus	Hoary fox	3.0-3.6	2.5-4.0		8
Speothos	venaticus	Bush dog			5-8	13
Urocyon	cinereoargenteus	Gray fox	2.0-3.9	3.4-5.5		14-15
•	littoralis	Island gray fox	1.3-2.4	1.4-2.5		[10]
Vulpes	bengalensis	Indian fox	>1.8	2.7-3.2		6-8
1	cana	Blanford's fox	0.8 - 1.5	0.8 - 1.4		6 [4-5]
	chama	Cape fox	2.0 - 4.0	2.0 - 4.2		
	corsac	Corsac fox	1.9-2.4	1.6-3.2		9
	ferrilata	Tibetan sand fox	3.0 - 4.1	3.8-4.6		
	macrotis	Kit fox	1.6-2.2	1.7-2.7		
	pallida	Pale fox			2.0-3.6	3
	rueppelli	Sand fox	1.1-1.8	1.1-2.3		6 [7]
	velox	Swift fox	1.6-2.3	2.0-2.5		[8]
	vulpes	Red fox	3.6-6.5	4.4-7.6		[9]
	zerda	Fennec fox	1.0-1.9	1.3-1.7		13-14

^aData from Kreeger et al., 2002; all other data from compiled information in Sillero-Zubiri et al., 2004.

Table 34.2. Analgesics used in non-domestic canids.

Drug	Dosage	Route	Species	Citation
Carprofen	4 mg/kg	Subcutaneous	Red fox	Brash, 2003
Buprenorphine	0.01-0.02 mg/kg	Intramuscular	Red fox	Brash, 2003
Butorphanol	0.1 mg/kg	Intravenous	Gray wolf	Nard, 1998
-	0.2 mg/kg	Intravenous	Maned wolf	McNulty et al., 2000
	0.4 mg/kg	Oral	Gray wolf	Nard, 1998
	0.2 mg/kg		Red fox	Brash, 2003
Morphine	0.05 mg/kg	Intravenous	Maned wolf	McNulty et al., 2000
Fentanyl	50 μg/hr	Dermal patch	Gray wolf	Nard, 1998
	75 μg/hr	Dermal patch	Maned wolf	McNulty et al., 2000

Small canids can be grabbed from behind and held by the scruff (Brash, 2003) or by grabbing around the neck, with the fingers closing underneath the jaws. If grabbing around the neck, care should be taken not to damage the trachea. At the same time that the neck is grabbed, the body is pushed firmly and gently against the ground by the handler or an assistant. Once in

hand, a muzzle can be applied using a small rope, gauze bandage, or tape. Caution must be used with muzzles because they impair the animal's ability to pant (see the preceding). If an animal appears overheated or distressed, the muzzle may need to be removed.

Appropriately sized squeeze chutes can be used for any canid, but care should be taken that the animal

cannot get its mouth or legs through the spaces in the chute. Many canids can be trained to walk into a chute.

VASCULAR ACCESS SITES

Arterial and venous access sites are comparable to those of domestic dogs. Medetomidine often causes vasoconstriction and may predispose to vasospasm, so vascular access may be more difficult with the use of this drug. Xylazine exerts similar changes, although vasodilation may follow the initial period of vasoconstriction. Venipuncture and catheterization should be done as soon as possible if medetomidine is used, preferably within the first 15 to 20 minutes post-induction, because vasospasm makes these procedures more difficult later during the immobilization. Typical sites for phlebotomy are the jugular, cephalic (brachial), and lateral saphenous veins. Venous catheters are typically placed in the cephalic or saphenous veins. For blood gas analysis, arterial samples are readily obtained from the femoral artery (Larsen et al., 2002).

ENDOTRACHEAL INTUBATION

Intubation of the anesthetized canid is not always essential, but should be performed during prolonged procedures (especially if inhalant anesthetics are used), or if animals are hypoxemic or hypoventilating. Intubation is as described for domestic dogs. Endotracheal sizes increase in proportion to the size of the animals: 3 to 4 mm for adult fennec foxes; 6 mm for adult red foxes (Brash, 2003); 9 to 10 mm for adult red wolves (Sladky et al., 2000); and 10 to 12 mm for adult grey wolves.

REVIEW OF IMMOBILIZATION AGENTS USED IN NON-DOMESTIC CANIDS

Dissociative Agents

The dissociative anesthetic, ketamine, is a mainstay of canid anesthesia. Tiletamine is also commonly used, but this drug is only available in combination with zolazepam (in Telazol) and recoveries are typically long with this drug combination. Phencyclidine was commonly used many years ago (Seal and Erickson, 1969), but is no longer available. Ketamine has been used alone to immobilize African hunting dogs, grey wolves, coyotes, red foxes, grey foxes, and kit foxes (Ebedes and Grobler, 1979; Jessup, 1982; Kreeger and Seal, 1986a). Induction times are rapid (3–6 minutes), but immobilization times are short (18-22 minutes) relative to recovery times (50-90 minutes) (Kreeger and Seal, 1986a). Typically only light anesthesia is achieved, but heart rate and respiratory rate are stable (Ebedes and Grobler, 1979). Increasing dosages do not decrease induction times or substantially increase immobilization times, but recoveries are longer (Jessup, 1982).

If used alone, dissociative agents induce rough inductions and recoveries, hyperthermia, skeletal muscle hypertonicity, muscle spasms, uncontrolled head movements, ptyalism, and convulsions (Jessup, 1982; Kreeger, 1992), so they are typically combined with α_2 -agonists, benzodiazepines, and/or opioids. Dissociatives cannot be antagonized, although yohimbine was tried in grey wolves (Kreeger and Seal, 1986a). Wolves that received yohimbine had their heads up more quickly, but took longer to stand than those receiving a placebo (Kreeger and Seal, 1986a). If ketamine is given with other agents that can be antagonized, the antagonists should not be administered until most of the dissociative has been metabolized. Early reversal may result in convulsions, tremors, hyperthermia, or rough recoveries because of residual ketamine. A 45-minute wait generally appears adequate. Waiting times seem less critical with the use of Telazol because zolazepam ameliorates the effects of the dissociative.

α₂-Adrenergic Agonists

 α_2 -Adrenoceptor agonists, including xylazine and medetomidine, are potent, reversible sedatives that are commonly used to smooth induction and recovery when either ketamine or tiletamine-zolazepam is used. Alone these agents can heavily sedate canids to the point of relatively safe handling, but these animals may also be aroused with stimulation and are capable of directed attack. For these reasons, it is usually preferable to combine an α_2 -agonist with at least one other drug.

Xylazine Xylazine has been used alone in wolves, coyotes, red foxes, grey foxes, and kit foxes (Philo, 1978; Jessup, 1982). Dosages need to be higher for excited animals because they have higher sympathetic tone that can override the adrenergic agonist. Use of xylazine alone is best for short procedures requiring only moderate handling (Kreeger et al., 1988); for longer or more stimulatory procedures, additional drugs are warranted. Initial effects occur in 2 to 3 minutes, animals are sternal in 4 to 10 minutes, and maximal effect is in 15 minutes (Philo, 1978). Induction is no quicker with higher dosages, but respiration is more depressed and there is a greater chance of apnea (Philo, 1978). Animals can be approached and safely handled if there are no loud noises and contact with the animal is not abrupt (Kreeger et al., 1988). Vomiting may occur shortly after xylazine administration (Philo, 1978; Jessup, 1982). Low heart rates may occur; historically, this has been counteracted by use of the anticholinergic drug, atropine (Philo, 1978), but low heart rates do not necessarily need to be treated if cardiac output and perfusion are good. Xylazine sedation typically lasts 30 to 60 minutes, but complete recovery takes 2 to 3 hours without reversal (Philo, 1978; Kreeger et al., 1988). Yohimbine is usually used for reversal, but tolazoline and atipamezole are other options. Recovery typically occurs 4 to 6 minutes

after intravenous (IV) administration of yohimbine (Kreeger et al., 1988).

Medetomidine Medetomidine is more potent and specific than xylazine. Like xylazine, high doses of medetomidine alone can effect complete immobilization in relatively calm canids. Complete immobilization was achieved in farmed Arctic foxes using 0.1 mg/kg (Jalanka, 1990). Similarly, calm, habituated grey wolves have been induced with 0.05 mg/kg. At high dosages, there is better muscle relaxation and less chance of spontaneous recovery, but mucous membranes may be cyanotic, oxygenation may be poor (as low as 74%), and respiration may be impaired (Kreeger et al., 1996). Second-degree atrioventricular heart blocks are common with the use of medetomidine and occur with increased frequency at higher doses. Atropine has been administered to relieve bradycardia; although the anticholinergic drug may double the heart rate, oxygen saturation does not necessarily improve. Without administration of reversal agents, immobilization with medetomidine lasts about 60 minutes (Kreeger et al., 1996). Recoveries are quick (2 to 5 minutes) with the administration of atipamezole (0.25 mg/kg, IV) and are slower if yohimbine (0.2 mg/kg, IV) is used (Kreeger et al., 1996). Although some sources advocate IV administration of atipamezole, we do not. Intravenous atipamezole appears to effect extremely rapid changes in cardiovascular parameters, with potentially deleterious consequences; such changes are not as rapid with IM atipamezole or IV yohimbine.

Phenothiazine Derivatives

The phenothiazine derivative, acepromazine is a tranquilizer that is occasionally used alone to calm canids that are trapped (5 mg/kg; McKenzie, 1993). Because acepromazine interferes with thermoregulation, it should not be used if ambient temperatures are high or traps are not checked frequently. Acepromazine is not effective alone as an immobilizing agent, but has occasionally been used successfully for South American canids in combination with ketamine (Pessutti et al., 2001).

Opioids

Some opioids can be useful in combination with other drugs for sedation, immobilization, and anesthesia. Butorphanol is used most often as it is inexpensive, has relatively mild respiratory effects, and is readily absorbed via intramuscular injection. Fentanyl and morphine have also been used. By itself, butorphanol has produced "apathetic sedation" in wolves (Kreeger, 1992). Anesthesia can be achieved when butorphanol is combined with an α_2 -agonist, but these combinations work best on calm, captive animals and are not potent enough to anesthetize free-ranging or otherwise highly excited canids (Kreeger, 1992).

Ultra-potent opioids (e.g., etorphine, carfentanil, sufentanil) have been used historically in large canids, but the human and animal hazards of these drugs, along with the availability of safer options, makes it less likely that they would be used for canids today.

Benzodiazepines

Benzodiazepines, such as diazepam, midazolam, and zolazepam are useful sedatives for facilitating muscle relaxation and preventing convulsions, particularly in combination with dissociative agents. They are also helpful in treating animals experiencing seizures or convulsions. Both diazepam and midazolam have been used with ketamine; zolazepam is combined with tiletamine in Telazol. Benzodiazepines are reversible with flumazenil; however, flumazenil is relatively expensive and in many situations, benzodiazepine reversal is probably not necessary. Benzodiazepines have minimal adverse cardiorespiratory effects and residual sedation is the most commonly observed occurrence post-immobilization. Flumazenil administration may be warranted in animals that are going through cardiorespiratory decompensation or when animals are to be immediately released into the wild after immobilization.

Combinations

Ketamine-Xylazine Ketamine-xylazine combinations were the standard protocols used for many canid species for several years. Small canids generally need higher dosages of ketamine than large canids, but dosages for xylazine tended to remain constant for different body weights. Some have advocated administration of xylazine 10 minutes prior to administration of ketamine (Cornely, 1979), but this is often impractical in the field setting and it is our experience that temporal separation of the drugs is not needed. Lower doses of ketamine with higher doses of xylazine result in quicker recoveries by taking advantage of the reversibility of the α_2 -agonist while minimizing the amount of ketamine that persists; quicker recoveries often occur even without reversal (Kreeger and Seal, 1986b). In coyotes, if the dosage of ketamine is decreased from 4 to 2 mg/kg, the recovery time is shortened from 2 to 3 hours to less than 1 hour (Kreeger and Seal, 1986b).

Induction with ketamine-xylazine is variable, occurring in 2 to 20 minutes; faster inductions occur when using relatively high dosages of ketamine and relatively low dosages of xylazine. Working times are typically 20 to 40 minutes, and complete recovery occurs in 1 to 2 hours (Cornely, 1979; Kreeger and Seal, 1986b). Heart rate may be either slowed or elevated; tachycardia is seen with high dosages of ketamine; bradycardia is seen with high dosages of xylazine (Kreeger and Seal, 1986b). Premature ventricular contractions (PVC) may occasionally occur, but do not typically cause clinical problems (Kreeger and Seal, 1986b). It is less common to see PVC arrhythmias if atropine is administered (Fuller and Kuehn,

1983), but it is more common to see hypertension and mean arterial blood pressures may be over 170 mmHg (Kreeger and Seal, 1986b). Because atropine exacerbates this hypertension without improving oxygenation, the use of an anticholinergic drug is usually contraindicated. Oxygenation is typically stable, but may be lower than desired (83%–94%; Osofsky et al., 1996). Blood pressure values tend to normalize after antagonists are administered (Kreeger et al., 1986). Respiratory rate is often elevated when ketamine-xylazine is used (Sladky et al., 2000). Canids immobilized with ketamine-xylazine have poor thermoregulatory ability and hyperthermia is also frequently observed (Fuller and Kuehn, 1983), although temperatures tend to decrease over the course of the immobilization (Sladky et al., 2000; Fuglei et al., 2002).

The xylazine component can be antagonized with yohimbine (0.1–0.2 mg/kg) or tolazoline (8 mg/kg) IV (Kreeger et al., 1986, 1990b), but antagonists should not be administered until 45 min after the last injection of ketamine; otherwise tachycardia, severe hypotension (less than 30 mmHg), mouth gaping, face scratching, twitching, and hyperreflexia may occur (Kreeger and Seal, 1986b). With yohimbine, arousal occurs in 1 to 8 minutes, sternal recumbency in 5 to 6 minutes, and uncoordinated ambulation in 10 to 25 minutes (Kreeger and Seal, 1986b). Doses of yohimbine higher than 0.2 mg/kg do not improve or hasten reversal, but instead cause ataxia, hyper-reflexion, tachycardia, and hypersalivation (Kreeger et al., 1990b). Yohimbine may be given IV, intramuscularly (IM), or a percentage by both routes (Osofsky et al., 1996).

Some immobilization-associated deaths have been reported with ketamine-xylazine, but the reasons for these deaths were not clear (Fuller and Kuehn, 1983).

Ketamine-Medetomidine In the past decade, many clinicians have switched from using ketamine-xylazine to ketamine-medetomidine. Much is similar about the two protocols; however, medetomidine is more potent and specific than xylazine so lower dosages of ketamine are effective and reversal is quicker and more complete. For canids, some authors have recommended ketamine (2.5–3 mg/kg) and medetomidine (0.06–0.1 mg/kg) for canids, in order to insure complete immobilization and operator safety (Jalanka and Röken, 1990); however, in our experience, slightly higher doses of ketamine (4–6 mg/kg) can be safely combined with lower doses of medetomidine (0.02–0.04 mg/kg) to provide effective immobilization with fewer adverse cardiopulmonary effects.

Animals are typically ataxic in 1 to 5 minutes, recumbent in 5 to 10 minutes, and induced in 10 to 15 minutes. Inductions may be much faster in captive animals that are accustomed to handling than in less acclimated individuals (Jalanka, 1990; Fuglei et al., 2002). Animals should be kept as calm as possible during induction. Vomiting occasionally occurs (Arnemo et al., 1993; Holz et al., 1996; Fuglei et al., 2002), particularly if animals

have not been fasted. Animals acclimated to handling and people may have stable body temperatures, but hyperthermia is common and temperatures tend to decrease over time (Jalanka, 1990; Arnemo et al., 1993; Sladky et al., 2000). Decline in body temperature may be substantial in raccoon dogs that are anesthetized during the winter when they hibernate; this decrease may critically affect their metabolism so special care to body temperature should be paid in this species (Arnemo et al., 1993).

Heart rate may increase or decrease over time in canids (Arnemo et al., 1993; Aguirre et al., 2000; Fuglei et al., 2000; Sladky et al., 2000). Heart rate is increased by atropine administration (Holz et al., 1994), but use of this drug is not typically warranted for the reasons described with ketamine-xylazine. Oxygenation is typically stable, but may be somewhat low. Arctic fox pups anesthetized with ketamine-medetomidine had $\rm SpO_2$ values of 78% to 95% (Aguirre et al., 2000), whereas mean values were 92% to 94% in red wolves (Sladky et al., 2000).

Respiratory rate tends to increase over time (Jalanka, 1990; Aguirre et al., 2000; Sladky et al., 2000). Raccoon dogs anesthetized with ketamine (5 mg/kg) and medetomidine (0.1 mg/kg) exhibited intermittent apnea and tachypnea, but breathing became more regular as time went on (Arnemo et al., 1993). These respiratory effects may have resulted from the relatively high dosage of medetomidine that was used.

Some authors have cited excess salivation as a reason for use of atropine in immobilization protocols (Holz et al., 1996). It is true that animals salivate less if an anticholinergic is administered; however, we have not appreciated hypersalivation to be a clinically important problem.

Ketamine-medetomidine immobilization typically lasts approximately 60 minutes after initial injection, although individual animals may rouse more quickly (Jalanka, 1990) and some animals do not regain corneal or pedal reflexes until greater than 120 minutes (Arnemo et al., 1993). Recovery is usually rapid, with animals standing 5 to 20 minutes post-antagonist and fully recovered 10 to 35 minutes post-antagonist (Jalanka, 1990; Arnemo et al., 1993; Aguirre et al., 2000). Without antagonist agents, complete recovery occurs in about 3 hours (Arnemo et al., 1993). Medetomidine is typically antagonized with atipamezole (5 mg/mg medetomidine (5:1) or 0.125 mg/kg). For most species, higher doses of atipamezole are contraindicated; foxes given 0.25 mg/kg atipamezole were reported to be nervous, over-alert, and developed muscle fasciculations (Jalanka, 1990). However, it is important to note that raccoon dogs were not effectively antagonized when given 5:1 atipamezole:medetomidine and 10:1 was needed instead (Arnemo et al., 1993). Although this dosage is higher than for any other canid, it did not cause raccoon dogs to be excited or overly alert (Arnemo

et al., 1993). Antagonism may be quicker with IV administration of atipamezole than with IM delivery, but the difference is a matter of 2 to 5 minutes. In blue foxes, IV atipamezole caused a 200% increase in heart rate 1.5-minutes post-administration (Jalanka, 1990). Given the rapid and dramatic changes in blood pressure and cardiovascular output that occurs when atipamezole is given IV, this route of administration poses unnecessary risks and should not be performed.

Unexplained mortalities have been seen with use of ketamine-medetomidine. Of 20 Arctic foxes anesthetized with ketamine (3 mg/kg)-medetomidine (0.05 mg/kg) for implantation of heart rate transmitters, two died 30 to 35 minutes into surgery (Fuglei et al., 2002). The cause of death was not explained, so surgical factors cannot be discounted.

Xylazine-Butorphanol Butorphanol (0.4 mg/kg) has been combined with xylazine (2 mg/kg) to immobilize grey wolves (Kreeger et al., 1989). Animals were induced in 12 minutes; bradycardia, respiratory depression, and normotension were observed. Immobilization was rapidly antagonized with yohimbine and naloxone. After antagonists were administered, heart rate and respiratory rate rapidly increased (Kreeger et al., 1989).

Medetomidine-Butorphanol Butorphanol has also been combined with medetomidine in canids; this drug combination can be fully antagonized, with few side effects, but requires minimal visual and auditory stimulation in order to be effective. Medetomidine (0.04 mg/kg) with butorphanol (0.4 mg/kg) was successfully used to immobilize 23 of 24 red wolves (Larsen et al., 2002). Induction times were 5 to 15 minutes. Some wolves received supplemental diazepam (0.2 mg/kg, IV) at induction, others received ketamine (1 mg/kg, IV) 30 minutes post-induction, and others received no additional anesthetics. A few red wolves experienced bradycardia (less than 40 beats per minute); heart rate and blood pressure increased when ketamine was given. Second-degree heart block and sinus arrhythmia were observed, but there were no other cardiac arrhythmias. Initial blood pressure values were high (98-194 mmHg), but decreased over time. Oxygenation was initially poor in a few animals, but improved over time and was generally good (SpO₂ greater than 93%). Effects of the medetomidine-butorphanol lasted 30 to 40 minutes; longer recumbency times were achieved with addition of diazepam or ketamine. Antagonism with atipamezole (0.2 mg/kg)-naloxone (0.02 mg/kg) effected quick recovery times, with animals fully recovered in about 7 minutes. Flumazenil (0.04 mg/kg) was also administered to wolves that had received diazepam. When low doses of glycopyrrolate were added, there appeared to be a threshold effect on heart rate and blood pressure. At low doses (0.0025-0.005 mg/kg) heart rate and blood pressure did not change, but at higher doses (0.0075-0.0175

mg/kg) acute tachycardia and severe sustained hypertension occurred (Larsen et al., 2001).

Xylazine-Fentanyl Similar to xylazine-butorphanol, xylazine (1 mg/kg)-fentanyl (0.1 mg/kg) has been used successfully to immobilize canids, African wild dogs in particular (de Villiers et al., 1995; Hattingh et al., 1995). This combination can be antagonized with yohimbine (0.125 mg/kg) and naloxone (1.2 mg per animal). Animals were ataxic in 1.5 to 3 minutes and recumbent in 5 to 7.5 minutes (Hattingh et al., 1995). If approached too soon, animals would respond to touch by getting up and running with ataxia. With any α_2 -agonist-opioid combination, canids should be left as undisturbed as possible until 10 minutes post-darting. Immobilization with xylazine-fentanyl typically lasts 45 to 60 minutes. During this time, canids are normoxemic, but hypercapnic (pCO₂ = 64 mmHg) and acidemic (pH = 7.18-7.28). Supplementation with small doses of xylazine-fentanyl can extend the immobilization by 45 to 60 minutes. Once antagonists are administered (IV), complete antagonism occurs within 1 to 2 minutes (Hattingh et al., 1995). Detomidine-fentanyl has been used in African wild dogs in a similar manner (Hattingh et al., 1995).

Ketamine-Medetomidine-Butorphanol These three drugs have been combined together to take advantage of the properties of each agent while minimizing side effects. This combination was compared with ketamine-xylazine, ketamine-medetomidine, and ketamine-medetomidine-acepromazine in red wolves (Sladky et al., 2000). Although all combinations were effective, hypertension was not as severe in the ketamine-medetomidine-butorphanol group and recoveries were faster and smoother. In some animals, mild hypoxemia (SaO $_2 = 87\%$ –90%) was observed early in the procedures, but improved over time (Sladky et al., 2000). Although respiration rate was lower in this group, hypercapnia was not observed.

A recent study reported minimal hypertension with mild cardiac changes (first- and second-degree atrioventricular block, sinus arrhythmia, and depressed left ventricular systolic function) using a combination of ketamine (2 mg/kg)-medetomidine (0.03 mg/kg)-butorphanol (0.2 mg/kg)-acepromazine (0.02 mg/kg)-isoflurane (1%–2%) in grey wolves (Valerio et al., 2005). However, this report did not measure blood pressure or assess arrhythmias until 35 minutes post-injection, and recovery times were not reported, so it is difficult to compare these results to other investigations (Valerio et al., 2005; Guglielmini et al., 2006).

Ketamine-Midazolam This combination has been reported in red foxes, with induction times of 4 to 6 minutes and head-up times of 14 to 23 minutes. Compared with other drug regimens, inductions were longer and there were more spontaneous recoveries

(Kreeger et al., 1990c). Ketamine-midazolam has not been a combination that been extensively investigated for wild canids, probably because of the availability of Telazol, a relatively inexpensive, high concentration dissociative-benzodiazepine alternative.

Tiletamine-Zolazepam Tiletamine-zolazepam (Telazol) has been used in a wide variety of species and may be the preferred agent for helicopter captures or escape situations in which accurate dosing may be compromised and quick induction is essential. Induction in grey wolves was no shorter using 10 mg/kg versus 5 mg/kg (5–8 minutes), but arousal time was twice as long with the higher dose (Kreeger et al., 1990a). For helicopter captures, doses over 10 mg/kg may need to be used in order for wolves to be adequately induced (Ballard et al., 1991). Telazol has also been effectively combined with xylazine in wolves (Kreeger et al., 1995) and with medetomidine in dingoes (Vogelnest, 1999).

High stepping was often the first drug response observed, followed by disoriented gait, loss of use of hind legs, licking lips, loss of use of forelegs, loss of head and neck movement, nystagmus, and loss of tongue movement (Ballard et al., 1991). Extreme salivation may occur and mild seizures are not uncommon (Ballard et al., 1991; Van Heerden et al. 1991). Within reason, differences in Telazol dosages do not seem to have a substantial effect on heart rate, respiratory rate, blood pressure, or temperature. Working times are typically 60 to 90 minutes at these dosages and recovery time is highly variable (25 to 300 minutes) (Ballard et al., 1991). Complete recovery times have been reported to be as long as 5 to 6 hours with 5 mg/kg Telazol and some wolves have very rough recoveries with ataxia, paddling, falling backward, and severe mutilation (Kreeger et al., 1990a). When supplementing canids induced with Telazol, it is generally recommended to administer ketamine, rather than additional Telazol, if only injectable anesthetics are given. Supplemental ketamine has produced substantially shorter arousal times (30-45 minutes post-injection) than equivalent doses of Telazol (80–130 minutes post-injection) (Kreeger et al., 1990a).

FIELD TECHNIQUES AND STRATEGIES

Free-ranging canids are typically trapped before drugs are administered (Kreeger, 1992), although field-darting occurs in some cases. Box traps, padded-jaw traps, or offset-jawed foothold traps are typically used. Although coyotes do not usually fight a trap for long (Kreeger, 1992), other canids may fight against the trap frantically (especially when approached by humans) and may pull out of the trap and/or injure themselves. Leg fractures are common when steel-jawed traps are used to capture red foxes. Box traps may be used on naïve fox populations, but are ineffective on many red foxes. Leg snares may be

useful for this species (Jessup, 1982). Small leg snares will also capture coyotes and other canids. Leg snares are more likely to result in compromise of blood supply and edema of the paw, but are less likely than jawed traps to cause crushing, contusion, lacerations, or fractures. In colder climates, snares may result in frostbite-type lesions and should not be used. Always check for trap injuries when such means of capture are employed. A restraint pole and double leather gloves can be used to remove animals from traps (Jessup, 1982).

Animals in traps are sometimes administered oral medication through "tranquilizer tabs" (Balser, 1965). The device is attached to the jaw of the trap and the tablet is ingested when the animal bites at the trap, resulting in sedation. Such sedation may decrease the chance of the animal injuring itself, but is insufficient for handling (Jessup, 1982). This technique was originally described in coyotes using high doses of powderform diazepam (48–96 mg/kg) wrapped in semi-rotten cloth; ataxia often lasted 18 to 36 hours and sedation could last days (Balser, 1965). Some deaths have been reported using this technique, but it is unknown what effect the drug has had on mortality (Balser, 1965). Modifications to these "tranquilizer tabs" have since been made. One device includes a balloon with 3 ml of petroleum jelly, covered by two layers of gauze (Jessup, 1982). If the trap may get wet, the tabs can be sealed by dipping them repeatedly in a melted mixture of 25% refined beeswax and 25% paraffin wax (Balser, 1965). Tablets of diazepam (6-7 mg/kg), midazolam (3-4 mg/kg) or acepromazine (5 mg/kg) also have been used. Acepromazine interferes with thermoregulation, so this drug should not be used if trapping is conducted at high ambient temperatures or the traps are infrequently checked. When using tablets, doses are relatively high because of the likely loss of drug during chewing (Jessup, 1982).

Injectable anesthetic drugs are most commonly administered intramuscularly by hand injection, pole syringe, or dart. Hand injection during physical restraint should be performed in smaller species in order to avoid errant needle placement and unnecessary tissue trauma. Larger canids can be safely darted with a blowpipe or dart gun.

Grey wolves can be relatively safely pursued and darted from helicopters because they are large and inhabit areas with open country. For this type of a procedure, a pilot and a shooter are typically needed. Rapid projectile dart rifles are needed to insure accurate dart placement. Complications of helicopter darting may include pneumothorax secondary to inadvertent thoracic dart placement (Kreeger et al., 1995) or exhaustion. Coyotes have also been effectively captured in this manner (Baer, Severson, and Linhart, 1978); and with helicopter-launched net guns, although the impact of the net may cause mortality using this latter technique (Gese et al., 1987).

African wild dogs can be darted from a vehicle at a range of 15 to 30 m (Van Heerden 1993) and should be darted in the upper hind leg. Wild dogs can also be captured by using a helicopter to chase a pack into a funnelshaped boma. Jackals have occasionally been darted from vehicles to which they have been habituated, but trapping is a much more practical method of capturing these animals (McKenzie and Burroughs, 1993). Small animals such as foxes will not normally approach to within darting distances. These animals have small muscle masses and damage to vital organs is very possible, even with light darts (McKenzie and Burroughs, 1993). Bat-eared foxes may retreat into burrows if darted; they also have a bushy coat that makes accurate dart placement difficult, so darting is not recommended (McKenzie and Burroughs, 1993). In some cases, capture collars (Wildlink Capture Collar, Advanced Telemetry Systems, Isanti, MN) have been used to facilitate immobilization through the automated injection of drugs using a remote signal (Federoff, 2001).

Approach the recumbent animal quietly and cautiously. The ear seems to be one of the more sensitive parts of the canid body to stimulation, so attempting to elicit an ear twitch with a stick or pole can be a good way of assessing anesthetic depth. If an ear twitch is still present 10 to 15 minutes after agent administration, supplemental drugs may be warranted. However, keep in mind that some animals maintain an ear twitch despite being otherwise adequately immobilized, so supplement judiciously.

The animal should be placed in lateral recumbency with the head and neck extended to provide a clear airway. Respiratory rate and depth are the most important parameters to monitor. These should be checked immediately and monitored throughout the procedure. Body temperature should also be checked and the animal should be kept out of direct sunlight, if possible, to avoid hyperthermia. Efforts to cool the animal should be instituted if rectal temperature exceeds 40°C.

Once respiration and body temperature are evaluated, heart rate should be checked. Any necessary ophthalmic examination should be performed early in the procedure so that lubrication can be applied to the cornea and the eyes can be covered. Muzzling the animal and hobbling the legs may be necessary if the animal is only sedated or lightly anesthetized.

Regular monitoring should be performed, with respiratory rate and depth assessed constantly. Heart rate and body temperature should be evaluated every few minutes. Portable monitors that gauge blood pressure, peripheral oxygen saturation, end-tidal carbon dioxide, and electrocardiograph profile are quite helpful in better monitoring each patient. These portable devices can be expensive and are not always essential for procedures (especially field immobilizations), but they tend to work well in canids of all different sizes and may contribute substantially to good anesthetic management. Their use

would be more important for prolonged procedures, clinical settings, and high-risk animals.

RECOMMENDATIONS

As with any group of animals, drugs used for immobilization of canids vary by the species and situation, as well as the preferences and experience of personnel.

For small canids, induction and maintenance with isoflurane is an easy way of quickly providing anesthesia from which animals can rapidly recover. Animals can either be manually restrained and induced via face cone or induced via chamber. Mask induction can be accomplished with animals up to the size of red wolves and coyotes, if there are trained personnel capable of good manual restraint. Chamber induction can occur in purpose-built plastic induction chambers or by placing a plastic bag around a transport kennel. When using these devices the patient must be closely monitored to insure that the animal does not have complications or become over-anesthetized. Animals can become overheated in induction chambers, so these devices should not be used if temperatures cannot be controlled. Some people prefer to use clear bags when placing plastic bags around kennels, so that the animals can be observed throughout induction. By using isoflurane induction, there is increased risk of exposure of personnel to inhalant anesthetics.

Isoflurane can also be used for maintenance of anesthesia. Animals may be maintained with a face mask over the mouth or through an endotracheal tube after intubation. There will be less environmental release of isoflurane if an endotracheal tube is used. Intubation is recommended for animals with complications or for any prolonged immobilization procedure. Sevoflurane can probably be used with equal efficacy and safety, but there is less experience with this drug as it has been more expensive and requires a vaporizer with different calibration settings.

Injectable anesthetic drugs may also be used safely and are particularly appropriate for larger canids and for remote anesthetic delivery. Recommended dosages from the literature are listed in Table 34.3.

Although there have been many anesthetic combinations recommended in the literature (see previous section), the following list only incorporates those that we recommend. These recommendations are based on literature reports, current drug availability, and personal experience.

For most routine procedures, on young healthy animals in a controlled environment, we recommend medetomidine-butorphanol. This combination provides profound sedation and 45 to 60 minutes of working time for most canids. Induction times with medetomidine-butorphanol are typically 5 to 15 minutes; it is not a highly potent combination, so this is not an appropriate combination for situations where

Alopex lagopus (Arctic fox)

Ketamine (2.5 mg/kg)-medetomidine (0.05 mg/kg); atipamezole (0.25 mg/kg) (Jalanka 1990; Aguirre et al., 2000)

Medetomidine (0.025-0.1 mg/kg) (Jalanka, 1990)

Telazol (10 mg/kg) (Kreeger et al., 2002)

Atelocynus microtis

Telazol (10 mg/kg) (Kreeger et al., 2002)

Canis audustus, Canis aureus, Canis mesomelas (Jackals)

Ketamine (5-8 mg/kg)-xylazine (0.5 mg/kg) (McKenzie and Burroughs, 1995)

Telazol (3-4 mg/kg, 6-8 mg/kg if not enclosed) (McKenzie and Burroughs, 1995)

Canis latrans (Coyote)

Ketamine (4 mg/kg)-xylazine (2 mg/kg); yohimbine (0.15 mg/kg) (Kreeger and Seal, 1986b)

Telazol (10-11 mg/kg) (Gray et al., 1974; Kreeger et al., 2002)

Canis lupus (Grey wolf)

Ketamine (3-4 mg/kg)-medetomidine (0.06-0.08 mg/kg); atipamezole (0.3-0.4 mg/kg IM) (Holz et al., 1994; Kreeger et al., 2002)

Medetomidine (0.05 mg/kg); atipamezole (0.25 mg/kg IM) (Kreeger et al., 1996)

Xylazine (2 mg/kg)-butorphanol (0.4 mg/kg); yohimbine (0.125 mg/kg IV)-naloxone (0.05 mg/kg IV) (Kreeger et al., 1989)

Ketamine (4-10 mg/kg)-xylazine (1-3 mg/kg); yohimbine (0.15 mg/kg IV) (Kreeger et al., 1987; Kreeger, 1992)

Xylazine (2 mg/kg captive, 3-4 mg/kg wild); yohimbine (0.15 mg/kg IV) (Philo, 1978; Kreeger et al., 1988)

Telazol (10 mg/kg)-xylazine (1.5 mg/kg) (Kreeger et al., 2002)

Telazol (3-10 mg/kg, 10-13 mg/kg for helicopter captures) (Boever et al., 1977; Kreeger et al., 1987; Ballard et al., 1991;

Vilá and Castroviejo, 1994)

Canis lupus dingo (Dingo)

Telazol(1–2 mg/kg)-medetomidine (0.04 mg/kg) (Vogelnest, 1999)

Ketamine (7.5 mg/kg)-xylazine (1 mg/kg) (Wentges, 1975)

Telazol (7–10 mg/kg) (Vogelnest, 1999)

Canis rufus (Red wolf)

Medetomidine (0.04 mg/kg)-butorphanol (0.4 mg/kg), supplement with diazepam (0.2 mg/kg IV) or ketamine (1 mg/kg IV); atipamezole (0.2 mg/kg)-naloxone (0.02 mg/kg) ± flumazenil (0.02 mg/kg) (Larsen et al., 2001)

Ketamine (2 mg/kg)-medetomidine (0.02 mg/kg)-butorphanol (0.2 mg/kg); atipamezole (0.2 mg/kg) (Sladky et al., 2000)

Ketamine (2 mg/kg)-medetomidine (0.04 mg/kg); atipamezole (0.2 mg/kg) (Sladky et al., 2000)

Ketamine (8-10 mg/kg)-xylazine (2 mg/kg); yohimbine (0.1 mg/kg) (Sladky et al., 2000; Kreeger et al., 2002)

Telazol (10 mg/kg) (Kreeger et al., 2002)

Canis simiensis (Ethiopian wolf)

Telazol (2-7 mg/kg) (Sillero-Zubri, 1996)

Cerdocyon thous (Crab-eating fox)

Ketamine (10 mg/kg)-xylazine (0.5-1 mg/kg) (Pessutti et al., 2001)

Telazol (10 mg/kg) (Kreeger et al., 2002).

Chrysocyon brachyurus (Maned wolf)

Ketamine~(2.5~mg/kg)-medetomidine~(0.08~mg/kg); a tipamezole~(0.4~mg/kg)~(Kreeger~et~al.,~2002)~(0.25~mg/kg)-medetomidine~(0.08~mg/kg); a tipamezole~(0.4~mg/kg)~(Kreeger~et~al.,~2002)~(0.25~mg/kg)~(

Telazol (3–5 mg/kg), supplement with ketamine (25–50 mg) (Norton 1990; Deem and Emmons, 2005)

Ketamine (6-9 mg/kg)-xylazine (0.5-2 mg/kg); yohimbine (0.1-0.2 mg/kg) (Norton, 1990; Pessuitti et al., 2001).

Cuon alpinus (Dhole)

Telazol (10 mg/kg) (Kreeger, 1992)

Lycaon pictus (African wild dog)

Xylazine (0.7–1.1 mg/kg)-fentanyl (0.1 mg/kg); yohimbine (0.125 mg/kg)-naloxone (0.04 mg/kg), supplement with xylazine (10 mg)-fentanyl (0.5 mg) (van Heerden, 1993; de Villiers et al., 1995)

Ketamine (3-5 mg/kg)-medetomidine (0.05-0.1 mg/kg); atipamezole (0.15 mg/kg) (van Heerden, 1993; Cirone et al., 2004)

Ketamine (1.6 mg/kg)-xylazine (2.2 mg/kg); yohimibine (0.2 mg/kg IV/IM) (Osofsky et al., 1996)

Telazol (1–4 mg/kg, wild more sensitive than captive) (van Heerden, 1993; Hattingh et al., 1995)

Nyctereutes procyonoides (Raccoon dog)

Ketamine (5 mg/kg)-medetomidine (0.1 mg/kg); atipamezole (1 mg/kg), (Arnemo et al., 1993)

Telazol (7 mg/kg) (Gray et al., 1974)

Otocyon megalotis (Bat-eared fox)

Ketamine (5-8 mg/kg)-xylazine (0.5 mg/kg) (McKenzie and Burroughs, 1993)

Telazol (5 mg/kg) (McKenzie and Burroughs, 1993)

(Continued)

Table 34.3. (Continued)

Pseudalopex culpaeus (South American fox)

Telazol (10 mg/kg) (Kreeger, 1992)

Pseudalopex vetulus (Hoary fox)

Ketamine (3–5 mg/kg)-xylazine (0.6–0.8 mg/kg) (Pessutti et al., 2001)

Speothos venaticus (Bush dog)

Telazol (10 mg/kg) (Pessutti et al., 2001).

Urocyon cinereoargentus (Grey fox)

Ketamine (11–15 mg/kg)-xylazine (2–3 mg/kg) (Jessup, 1982) Telazol (9 mg/kg) (Gray et al., 1974)

Vulpes chama (Cape fox)

Ketamine-xylazine (5–8 mg/kg and 0.5 mg/kg) (McKenzie and Burroughs, 1993) Telazol (5–mg/kg) (McKenzie and Burroughs, 1993)

Vulpes macrotis (Kit fox)

Telazol (10 mg/kg) (Kreeger et al., 2002)

Vulpes pallida (Pale fox)

Telazol (10 mg/kg) (Kreeger, 1992)

Vulpes velox (Swift fox)

Ketamine (10 mg/kg)-xylazine (1 mg/kg); yohimbine (0.125 mg/kg) (Telesco and Sovada, 2002) Telazol (10 mg/kg) (Kreeger et al., 2002)

Vulpes vulpes (Red fox)

Ketamine (4 mg/kg)-medetomidine (0.02 mg/kg)-butorphanol (0.04 mg/kg), reversed with atipamezole (0.1 mg/kg) (Brash, 2003) Ketamine (25–30 mg/kg)-midazolam (0.6 mg/kg) (Kreeger et al., 1990b; Kreeger et al., 2002) Ketamine (20–23 mg/kg)-xylazine (1–1.2 mg/kg); yohimbine (0.15 mg/kg) (Kreeger et al., 1990c; Brash, 2003) Telazol (4–10 mg/kg) (Boever et al., 1977; Kreeger et al., 1990c; Brash, 2003)

Vulpes zerda (Fennec fox)

Telazol (10 mg/kg) (Kreeger et al., 2002)

Drugs or drug combinations are listed in order in which they are recommended.

the animals are uncontained, such as darting from a helicopter. One of the authors prefers to use medetomidinebutorphanol for short procedures in medium-to-large Canis spp. (wolves, red wolves, coyotes) particularly in situations where the animal is to be released immediately back into the wild (RSL). Medetomidine-butorphanol induces profound sedation, and procedures such as phlebotomy, radio collar attachment, measurements, and skin biopsies can be performed. However, this combination should not be used for more invasive procedures as there is no general anesthetic incorporated. It should be noted that there is a small subset of the population that will not be adequately immobilized with this combination. For these animals, small amounts of another agent, such as ketamine, diazepam, or midazolam, may be needed. If ketamine is used, atipamezole-naloxone should not be administered for 30 to 45 minutes, but there is still rapid, smooth recovery.

In a less controlled situation, such as emergency captures or helicopter darting, Telazol, ketamine-medetomidine, or ketamine-xylazine may be more appropriate since there is a lower volume of drug and induction is more rapid. Induction with medetomidine-butorphanol is often 10 to 15 minutes, whereas induction with Telazol is typically less than 5 minutes.

In animals that are ill or aged, particularly if cardiac or respiratory disease is suspected, it is probably not advisable to use medetomidine or other α_2 -agonists. Although these agents can be rapidly antagonized, their effects on blood pressure, heart rate, and respiration make them unnecessarily risky in high-risk patients. For compromised patients, inhalant induction may be the safest option. However clinical judgment must be used to determine if the stress of handling will be detrimental to the animal's condition. Injectable combinations such as ketamine-midazolam, ketamine-midazolambutorphanol, or Telazol can also be used.

COMPLICATIONS

Respiratory depression is a common complication for immobilized canids, and can be induced by α_2 -adrenoceptor agonists or opioids. Respiratory depression often manifests as hypoxemia and hypercapnia. Hypoxemia can be addressed by providing supplemental oxygen in the nares or through an endotracheal tube. Hypopnea and hypercapnia may be corrected through intubation and assisted ventilation. Opioids and α_2 -agonists may be antagonized, but the animal may not remain anesthetized and effects from residual

dissociative agents may occur. A respiratory stimulant, such as doxapram, may increase respiratory rate and ventilation, at least transiently.

Prolonged exertion may result in hyperthermia, which needs to be treated quickly. Heavily furred animals can also become hyperthermic when under a warm sun, even with cold ambient temperatures. Most canids dissipate heat through panting, which is often compromised during immobilization. Hyperthermia should be suspected if rectal temperature is greater than 40°C and treatment is mandatory if the temperature is greater than 41°C. Move hyperthermic animals out of direct sunlight. Cooling measures may be warranted such as spraying the body with water, packing with icepacks, application of isopropyl alcohol to proximal legs and ears, cold water enemas, and administration of cool IV fluids. Be careful to remove these cooling methods as body temperature declines in order to prevent hypothermia.

Hypothermia occasionally occurs under cold conditions, prolonged immobilizations, or in animals with hair loss or debilitated body condition. Warm water containers, warm blankets, heat pads, heat lamps, and hand warmers can be used to increase body temperature. Recovery will be slowed if the animal remains below normal body temperature.

Severe sustained hypertension may be seen with concurrent use of dissociative agents and α_2 -adrenoceptor agonists. Ketamine-medetomidine-induced hypertension can be particularly severe, but this can also be seen with ketamine-xylazine or with α_2 -agonists in the absence of a dissociative agent (Kreeger et al., 1986; Sladky et al., 2000; Larsen et al., 2002). Blood pressure typically declines over time and is less severe in calm animals. Anticholinergics should be used judiciously to avoid exacerbating hypertension. The use of anticholinergic drugs with α_2 -agonists can cause significant cardiovascular side effects.

Vomiting may occur and can result in aspiration of stomach contents. To prevent this problem, captive animals should be fasted 12 to 24 hours prior to immobilization, but this is not an option for freeranging animals. Water can be withheld up to 12 hours in advance, but 2 hours is typically sufficient. Vomiting upon recovery is typically less hazardous than at induction because the animal has control of its glottis and is less likely to aspirate. If an animal vomits when anesthetized, it should be placed in sternal recumbency with the neck extended and the nose pointed down.

Seizures may occur with the use of dissociative anesthetics, although they may be seen with less frequency as lower doses of dissociatives are used and as benzodiazepines are more commonly used as part of immobilization combinations. If the animal only experiences one or two short seizures, treatment is not necessary, but if more seizures occur, or if seizures are sustained, diazepam or midazolam should be administered IV or IM. Remember

to administer diazepam over 10 to 20 seconds IV to prevent cardiac arrest from the propylene glycol.

Wounds are common and should be treated with appropriate medical care. Also, traumatic injuries can occur from misplaced darts. All anesthetized canids should be checked for wounds from traps, needles, and conspecifics. Removal of hair should be minimized if the coat is needed for thermoregulation.

Rare complications in canids include cardiac arrest and gastrointestinal dilatation and volvulus.

There is much discussion in the literature regarding the stress of capture and immobilization of African wild dogs, with speculation that handling-induced stress contributed to mortality in this species through elevated corticosteroids and recrudescence of latent viruses. The evidence for this is scant and analysis of the pertinent data suggests that handling does not increase the likelihood of disease in this species (de Villiers et al., 1995).

RECOVERY

The immobilized animal should not be left unattended until it has recovered, unless it is in captivity or held such that it can be kept away from other animals and hazards. Monitoring should intensify when hazards such as water and precipices are in the immediate area. For these reasons, immobilization combinations that can be antagonized are ideal. Yohimbine may be given IV to rapidly antagonize xylazine; similarly, naloxone or naltrexone may be given IV to antagonize butorphanol. Some authors advocate IV atipamezole, but this may put undue strain on the cardiovascular system because of the drug's potent and specific nature. Atipamezole IM appears to result in acceptably swift recovery times. Once antagonists are administered the animal should be left undisturbed in a shaded quiet area; if moved after antagonists are administered, the animal may become agitated and tend to stand and run before having fully recovered. Also, canids can often be allowed to recover in kennels or crates. Safety precautions should be taken when releasing the recovered animals so that they do not injure handlers.

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35 Bears Nigel Caulkett

GENERAL CONSIDERATIONS FOR ANESTHESIA OF BEARS

Bears are not particularly prone to complications during anesthesia. In the wild, they are often subject to physical restraint via snares or traps prior to anesthesia. Physical restraint can result in stress, hemoconcentration, or injury (Cattet et al., 2003a). A careful physical should be performed as part of any capture to identify capture-related injuries. Bears are monogastrics, as such, they are prone to vomiting on induction, or regurgitation during anesthesia. It is best to avoid anesthetizing bears that have recently eaten. This is not always possible in management situations, but may be an option in research situations, and should be adhered to with captive animals.

Human safety must always be considered during capture and anesthesia of bears. It is important to know the behavior of the target species. With free-ranging bears it is also important to consider other bears in the vicinity. These animals can pose a threat to the anesthetized bear or the capture personnel.

CAPTURE OF WILD BEARS

There are two major methods to facilitate capture of wild bears. In open areas, such as tundra or alpine meadows, bears can be pursued and darted from a helicopter. In forested areas, bears are generally captured by physical means prior to anesthesia. Management situations may dictate that a free-ranging animal is darted by a ground-based capture team. These situations can be risky as there is a possibility that the capture team will lose track of the animal during the induction period.

Aerial Capture

Aerial capture techniques are best suited for capture of polar bears (*Ursus maritimus*), and brown bears (*Ursus arctos*). The animal is located, pursued, and the dart is

delivered at close range. It is important to assess the terrain for any hazards prior to pursuit. The major complications encountered with this technique are hyperthermia and acidosis (Cattet et al., 2003a). The risk of these complications can be minimized by keeping pursuit and induction times as short as possible.

Physical Restraint

In forested areas aerial capture is generally not a safe option. Physical capture techniques are often employed in these situations. The two most common methods are culvert traps and snares. Following physical capture the animal may be anesthetized without the risk of losing it in a forest environment. Bears captured in culvert traps may experience hemoconcentration (Cattet et al., 2003a). Brown bears captured with snares demonstrated a stress leukogram, hemoconcentration, and muscle damage, evidenced by elevations in serum muscle enzymes (Cattet et al., 2003a). Snared bears often exhibit increased serum myoglobin, and pathological lesions indicative of capture myopathy have been observed (Cattet et al., 2005). Fractures and soft-tissue injuries may also be encountered in snared animals. Snares should be checked frequently, to minimize time spent in the snare, and snared animals should be closely examined to identify and treat snare-related injuries.

DRUG DELIVERY

Drug delivery systems must be reliable and accurate. Systems that have low impact energy and deliver drugs at a low velocity are generally preferable. Captive bears may be injected with a pole syringe or blow dart. Volume limitations with blow darts necessitate the use of potent drug combinations for large bears. Large aggressive bears, captured in snares, may be darted via a pneumatic pistol. It is advisable to dart free-ranging bears from a safe distance. Cartridge or CO₂-powered rifles facilitate drug delivery in these situations.

Potent drugs may be incorporated into a sticky bait, to facilitate capture in zoological settings.

Many bear species demonstrate seasonal variation in fat distribution. Black bears and brown bears deposit a thick layer of fat over the rump in fall, and the shoulder or neck is the preferred location for dart placement. In spring, these animals can be darted in the hind quarters. Polar bears may have a thick layer of fat at any time of the year and the shoulder or neck should be targeted.

MONITORING ANESTHESIA AND SUPPORTIVE CARE

Anesthetic Depth

Depth of anesthesia should be closely monitored as some drug combinations have proved to be unreliable in bears. Sudden recoveries have been encountered with xylazine-ketamine and medetomidine-ketamine (Jalanka and Roeken, 1990; Cattet et al., 1999a). These combinations are best avoided in most situations. Factors that increase the risk of sudden arousal include: loud noise, particularly distress vocalization of cubs (Jalanka and Roeken, 1990). Other factors that can induce arousal include movement of the bear (e.g., changing the body position or location of the anesthetized animal) or painful stimuli, such as tooth extraction.

Techniques for monitoring depth of anesthesia depend on the agent used. Tiletamine-zolazepam (Telazol, Zoletil (ZT)) produce reliable anesthesia with predictable signs of recovery. Lightening of anesthesia is evidenced by: spontaneous blinking, chewing, and paw movement. As the depth of anesthesia further decreases, animals demonstrate head movement. Animals with significant head movement generally require a "top-up" of tiletamine-zolazepam or ketamine, unless they are to be left to recover. Top-up doses of tiletamine-zolazepam can significantly prolong recovery, and should only be used if more than 30 minutes of additional anesthetic time is required. Ketamine is a better choice if 5 to 20 minutes of additional time are needed.

In xylazine-ketamine or medetomidine-ketamine anesthetized bears, head lifting or limb movement signal that the bear is extremely light and should not be approached or manipulated. Increased intensity of the palpebral reflex or nystagmus are early indicators that the bear is light.

With both xylazine-zolazepam-tiletamine (XZT) and medetomidine-zolazepam-tiletamine (MZT), head lifting should be absent before the bear is approached. The palpebral reflex can be used to determine depth of anesthesia. Lightly anesthetized bears begin to breathe deeply, and may sigh. They may start to lick, and develop a spontaneous palpebral reflex. Head lifting or paw movement should be a sign to be extremely cautious, as the bear may soon rouse.

Cardiovascular Monitoring and Support

The cardiovascular system should be closely monitored. Polar bears, black bears, and brown bears anesthetized with ZT commonly have heart rates of 70 to 90 beats per minute (bpm). Heart rate is slightly lower with XZT and MZT, 50 to 70 bpm. Bradycardia is common with medetomidine-ketamine, heart rates of 30 to 40 bpm are not uncommon in polar bears. The femoral artery is the best location to palpate a pulse, but the brachial artery can also be used. Blood can be sampled from the jugular or medial saphenous vein. IV catheters may be placed in the jugular or cephalic vein (Figure 35.1).

Blood pressure can be measured directly from the femoral artery. Oscillometric monitors can be useful in smaller bears. The cuff width should be approximately 0.4 times the limb circumference. Mean arterial pressure in polar bears anesthetized with TZ was approximately 150 mmHg (Caulkett et al., 1999). Polar bears anesthetized with MZT are hypertensive (MAP greater than 200 mmHg) (Caulkett et al., 1999). Black bears are also hypertensive with this combination (Caulkett et al., 1997).

Respiratory Monitoring and Supportive Care

Bears are not particularly prone to hypoxemia under anesthesia. Oxygenation under tiletamine-zolazepam is generally good, but the addition of an α_2 -agonist can result in hypoxemia.

Oxygenation is best monitored with a pulse oximeter. The pulse oximeter probe can be placed on the tongue (Figure 35.2).

This may be difficult in bears lightly anesthetized with ZT, as they tend to chew. A hemoglobin saturation of less than 85% is indicative of hypoxemia, which can generally be treated with supplemental inspired oxygen (Figure 35.3).



Figure 35.1. Grizzly bear, with intravenous catheter placed in the cephalic vein.



Figure 35.2. Placement of a multisite pulse oximeter probe on a black bear.



Figure 35.3. Grizzly bear receiving supplemental inspired oxygen.

Portable equipment is available to facilitate oxygen delivery. An ambulance-type regulator and aluminum D-cylinder is lightweight, portable, and sturdy. It can be carried in a backpack and will provide a 10-L/minute flow for up to 30 minutes. An E-cylinder will provide this flow for 1 hour or more. A nasal catheter is a simple method to provide supplemental inspired oxygen. The catheter should be threaded as far as the medial canthus of the eye. A flow rate of 5 to 10 L/minute is required in most bears. Efficacy of oxygen therapy can be monitored with a pulse oximeter. Oxygen flow can be adjusted to maintain a saturation of 95% to 98% with the minimum required oxygen flow.

Intubation of bears is not difficult. The oral and pharyngeal anatomy is similar to that of a canid. Intubation is easiest with the bear positioned in sternal recum-



Figure 35.4. Brown bear positioned on a stretcher prior to weighing. (Courtesy of Gordon Sternhouse.)

bency. A laryngoscope facilitates visualization of the glottis prior to intubation. Tube size is very dependent on size of the bear. We typically carry size 8 to 14 tubes for black bears and 8 to 18 for brown bears.

Body Temperature

Rectal temperature should be closely monitored. Rectal temperature tends to decrease over time with TZ. It tends to increase with XZT and MZT. In hot ambient temperatures body temperature can increase to dangerous levels (more than 41°C). In these situations the α_2 -agonist should be antagonized as quickly as possible.

Supportive Care

The eyes should always be lubricated, and caution must be exercised to avoid corneal abrasions or ulceration. A blindfold should be placed to protect the eyes and decrease visual stimuli.

Bears are best positioned in sternal recumbency, but can be positioned in dorsal or lateral recumbency, with few adverse effects.

When possible, anesthesia should be reversed in freeranging animals. This is particularly important for sows with cubs, and in areas where high concentrations of bears are present.

Translocation of bears in cargo nets, by helicopter can result in mortality (Cattet et al., 1999b). Slinging in a cargo net can induce hypertension and hypoxemia (Cattet et al., 1999b). Ideally, these bears should be transported or weighed with their head and neck extended and their body extended in sternal or dorsal recumbency (Cattet et al., 1999b). We have used a stretcher-type sling to facilitate this positioning. If bears are to be relocated in culvert traps they should be awake before transport (Figure 35.4).

PHARMACOLOGICAL CONSIDERATIONS

The following section deals with combinations that can be used to anesthetize bears. Mean dosages of these combinations can be found in Table 35.1.

Xylazine-Ketamine

This combination may be suitable for short procedures in small bears, but the risk of sudden arousal limits its utility in larger, more aggressive bears. Risks to the animal include convulsions and hyperthermia. Xylazine can be antagonized with yohimbine, but because a high dose of ketamine is required, adverse effects of the ketamine (rigidity, convulsions, and hyperthermia) are unmasked (Ramsay et al., 1985).

Medetomidine-Ketamine

The major advantages of medetomidine-ketamine over xylazine-ketamine are that small volumes are required, and because a low dose of ketamine is used, reversal of medetomidine does not result in rigidity or convulsions. This combination may be useful for small bears, but should not be used in larger potentially aggressive bears. Sudden recoveries have occurred in brown bears (Jalanka and Roeken, 1990), and polar bears (Cattet et al., 1999). This combination should only be used by experienced personnel, for short procedures, and depth of anesthesia should be closely monitored.

Zolazepam-Tiletamine (Telazol, Zoletil)

This drug combination produces reliable anesthesia in bears. Recovery is slow, smooth, and predictable. Zolazepam-tiletamine produces minimal adverse effects on the respiratory or cardiovascular systems; therefore, it has a high margin of safety (Caulkett et al., 1999). The major disadvantages of zolazepam-tiletamine are lack of analgesia (Caulkett et al., 1999) and lack of reversibility (Cattet et al., 1999a; Caulkett et al., 1999). Recovery can be prolonged, particularly in large bears, and if repeated doses are administered.

Medetomidine-Zolazepam-Tiletamine

This combination can be delivered in small volumes, which increases its utility in large polar or brown bears. MZT provides better analgesia than zolazepamtiletamine alone (Caulkett et al., 1999). The major advantage of the combination of the same of the combination of the combi

tage of this combination is that it is readily and rapidly reversible with atipamezole. The major disadvantages of MZT are hypertension and hypoxemia (Caulkett and Cattet, 1997; Caulkett et al., 1999). Hypoxemia can be offset by the provision of supplemental oxygen. MZT has been used in black bears (Caulkett and Cattet, 1997), polar bears (Cattet et al., 1999), and brown bears (Arnemo et al., 2001). Immobilization induced by MZT is readily antagonized with atipamezole at three to four times the medetomidine dose.

Xylazine-Zolazepam-Tiletamine

XZT has many of the same characteristics as MZT (Cattet et al., 2003b,c). It provides analgesia and can be delivered at approximately half the volume of Telazol alone. XZT produces hypertension and hypoxemia (Cattet et al., 2003b). Hypoxemia is generally not severe and responds well to supplemental inspired oxygen. XZT produces effective immobilization. It is important to note that quality of anesthesia is different from Telazol alone, and head lifting or limb movement may immediately precede arousal. This combination is potentially reversible with yohimbine or atipamezole. (Tolazoline appears to be ineffective.) Our current experience is that although recovery is not rapid, as with medetomidineketamine or MZT, it is still faster than with Telazol alone. The longer recovery is probably a result of the higher Telazol requirement with this mixture, compared with MZT. We generally use 0.1 to 0.2 mg/kg of yohimbine or 0.1 mg/kg of atipamezole to antagonize the xylazine component of this mixture.

Oral Carfentanil

Carfentanil has been used orally in captive bears. The drug is mixed in honey. The sticky base coats the mouth and allows for sublingual absorption. This method may be preferable in captive bears when injection is not desired (Mama et al., 2000). In black bears oral carfentanil produced effective immobilization that was accompanied by rigidity and muscle tremors (Ramsay et al., 1995). Diazepam was administered at a dose of 25 mg IV to treat these tremors (Ramsay et al., 1995). Bears immobilized with oral carfentanil were hypoxemic. This was readily treated with supplemental inspired oxygen (Ramsay et al., 1995). Oral carfentanil

Table 35.1. Mean recommended dosages of immobilizing agents used to facilitate capture of American black bears, brown bears, and polar bears.

Drug Combinations (Mean Dosage in mg/kg)	Black Bear	Brown Bear	Polar Bear
Xylazine/ketamine	2/4	NR	NR
Medetomidine/ketamine	0.04/1.5	NR	NR
Medetomidine/tiletamine-zolazepam	0.05/2	0.025/4.5	0.06/2.2
Xylazine/tiletamine-zolazepam	2/3	2.5/3.8	2/3
Tiletamine-zolazepam	7	8	8

NR, not recommended in this species.



Figure 35.5. Maintenance of anesthesia with isoflurane in a black bear.

has also been used as part of a balanced anesthetic technique in a brown bear (Mama et al., 2000).

Volatile Anesthesia

Volatile anesthesia may be required for invasive or prolonged procedures. The bear is induced with one of the discussed combinations, intubated, and maintained on volatile anesthesia delivered via an appropriately sized circuit. Bears under 150 kg body weight may be maintained on a small animal circle system. A large animal machine should be used for heavier animals. Isoflurane is a good choice for maintenance of anesthesia. Isoflurane-induced vasodilation tends to offset the hypertension that can result from administration of potent α_2 -agonists. The major side effects of isoflurane are hypotension and respiratory depression. It is advisable to monitor blood pressure and end-tidal or arterial CO_2 in bears anesthetized with isoflurane (Figure 35.5).

Recovery from isoflurane is generally smooth. α_2 -agonist drugs should be antagonized at the termination of surgery to hasten recovery.

SPECIES-SPECIFIC CONCERNS

Polar Bear (Ursus maritimus)

Polar bears can have substantial fat deposits throughout the year. The shoulder and neck are the best sites for drug delivery. Male polar bears can be large and heavy. Potent drug combinations are required to keep drug volume and dart size to a minimum. Polar bears should be positioned carefully to avoid excessive pressure on limbs that could result in compartment syndrome. Polar bears enter a hypometabolic state during the summer. At this time of the year animals are fasting and body temperature is decreased (34°C–35°C). Immobilizing drug requirements may also be decreased at this time of

year. In areas in which large numbers of polar bears congregate, reversible anesthetic protocols should be considered. This decreases the risk of predation from other bears. Reversible protocols should also be considered for mother bears with cubs.

Zolazepam-tiletamine (Table 35.1) produces reliable immobilization, but can also result in prolonged recoveries. Volume requirements are high. This can produce excessive tissue trauma and necessitate the use of large darts.

Xylazine-zolazepam-tiletamine (Table 35.1) can be delivered at approximately half the volume of zolazepam-tiletamine alone. It is potentially reversible with yohimbine or atipamezole. Reversal of this mixture is not reliable. This is probably owing to residual zolazepam-tiletamine sedation. Animals immobilized with this mixture benefit from supplemental inspired oxygen.

Medetomidine-zolazepam-tiletamine (Table 35.1) produces reliable as well as rapid-onset immobilization. It can be delivered in a small volume and is readily reversible with atipamezole administered at four times the medetomidine dose. Animals benefit from supplemental inspired oxygen (Caulkett et al., 1999).

Brown Bear (*Ursus arctos*)

A variety of techniques can be used to anesthetize brown bears. Drug combinations should be reliable and potent. Brown bears enter a hypometabolic state in the winter. Drug requirements may be decreased at this time.

Zolazepam-tiletamine (Table 35.1) is routinely used for management of brown bears in North America. Reversible combinations are desirable in certain situations, particularly in free-ranging sows with cubs.

Zolazepam-tiletamine produces reliable immobilization, but can also result in prolonged recoveries. Volume requirements are high, this can produce excessive tissue trauma, and necessitates the use of large darts.

Xylazine-zolazepam-tiletamine (Table 35.1) is potentially reversible with yohimbine or atipamezole. Reversal of this mixture is not reliable. This is probably owing to residual zolazepam-tiletamine-induced sedation. Animals immobilized with this mixture benefit from supplemental inspired oxygen.

Medetomidine-zolazepam-tiletamine induces a rapid onset of immobilization, can be delivered in a small volume, and is readily reversible with atipamezole administered at five times the medetomidine dose. MZT is used for immobilization of Scandinavian brown bears (Arnemo et al., 2001). The dosage ranges from 35 $\mu g/kg$ of medetomidine +4.8 mg/kg of zolazepam-tiletamine in yearlings to 20 $\mu g/kg$ of medetomidine +4.7 mg/kg of zolazepam-tiletamine in adult males.

Oral carfentanil has been used at a dose of $8 \mu g/kg$ in a captive brown bear. This dose induced deep sedation sufficient for intubation. The bear also received

0.02 mg/kg of atropine IM. Naltrexone was administered at a dose of 0.42 mg/kg IM and IV to speed recovery (Mamma et al., 2000).

American Black Bears (Ursus Americanus)

These bears have a more placid nature than brown bears; dose requirements are lower with zolazepam-tiletamine. A variety of drugging techniques can be used. Black bears are frequently immobilized for management purposes in North America. The bear may be snared or captured in a culvert trap prior to drug administration. Physical capture of the bear facilitates drug administration and limits mobility on induction. Free-ranging bears are often treed prior to drug administration. This also facilitates drug administration and decreases mobility on induction. Ideally, a coniferous tree should be chosen, as the boughs will help to break the bear's fall on induction. Air-filled bags or mattresses can be placed at the base of the tree to soften the landing. Bears that remain in the tree, after induction, may need to be placed in a sling and lowered with ropes.

Zolazepam-tiletamine (Table 35.1) produces reliable immobilization and can be delivered at a relatively low volume in most bears.

Xylazine-zolazepam-tiletamine (Table 35.1) is a useful combination in black bears. The dose we have used is similar to a brown bear or polar bear dose. It is possible that the dose could be lowered. Further work is needed to determine an appropriate dose for this species.

Medetomidine-zolazepam-tiletamine (Table 35.1) induces a rapid onset of immobilization, can be delivered in a small volume, and is readily reversible with atipamezole, administered at four times the medetomidine dose. Animals will benefit from supplemental inspired oxygen(2).

Xylazine-ketamine (Table 35.1) can be used cautiously in black bears. It is important to monitor the bear closely for signs of arousal. Rapid nystagmus and brisk tongue withdrawal are signs of light anesthesia. An IV top-up of xylazine-ketamine at one-third the original dose may be considered, or procedures may be terminated.

Oral carfentanil has been used in captive black bears. A dose of 6.8 to 18 μ g/kg is administered in honey. Bears demonstrated muscle rigidity, which was readily treated with diazepam (10–25 mg IV). Bears also developed hypoxemia that resolved with 5 L/minute of supplemental oxygen (Ramsay et al., 1995).

Sloth Bear (*Melurus ursinus*), Sun Bear (*Ursus malayanus*), Asiatic Black Bear (*Ursus thibetanus*), Spectacled Bear (*Tremarctos ornatus*), and Giant Panda (*Ailuropda melanoleucia*)

These species are grouped at the end of the section because there is a paucity of information in the literature about anesthesia of these animals. It is very

probable that xylazine + zolazepam-tiletamine and medetomidine + zolazepam-tiletamine or oral carfentanil are as effective in these species as in other bear species. Zolazepam-tiletamine has been used in sun bears at a dose of 4.0 to 5.5 mg/kg, in sloth bears at a dose of 5.5 to 6.6 mg/kg, in Asiatic black bears at a dose of 2.8 to 4.4 mg/kg, and in spectacled bears at a dose of 3.2 to 11.1 mg/kg (Schobert, 1987). Sloth bears have been anesthetized with 1.4 to 2.4 mg/kg of xylazine, combined with 5.8 to 9.7 mg/kg of ketamine (Page, 1986). Sun bears have been anesthetized with 60 to 80 µg/kg of medetomidine + 2 to 3 mg/kg of ketamine (Jalanka and Roeken, 1990). Giant Pandas have been anesthetized with a variety of techniques. Ketamine (4.8 mg/kg) + xylazine (0.43 mg/kg) has been described as a suitable protocol for healthy pandas (Kreeger et al., 2002); alternatively, 5.8 mg/kg of tiletamine/zolazepam can be used (Kreeger et al., 2002).

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36

Procyonids and Mustelids

George Kollias and Noha Abou-Madi

INTRODUCTION

Chemical restraint and anesthesia techniques and protocols applicable to captive mammals in the families Mustelidae and Procyonidae are similar in many respects to the techniques used for domestic dogs and cats. Chemical restraint and anesthesia of free-ranging members of these families present challenges not dissimilar to those encountered for mammals in other families and genera, including the capture techniques employed and stress associated with capture and restraint. The metabolic impact of physical restraint and general anesthesia on animals is often underestimated. As an example, ferrets manually restrained showed significant increase in their plasma concentration of cortisol and adrenocorticotropic hormone (ACTH) and a decrease in α -melanocyte stimulating hormone (MSH), whereas isoflurane anesthesia resulted in significant increase in plasma MSH directly after induction (Shoemaker et al., 2003). Applying the basic principles of restraint and anesthesia are essential to ensure a successful outcome. Specialized equipment and supplies (small endotracheal tubes, special face masks, small intravenous and intraosseous catheters, and cannulas) should be on hand at the outset of the procedure. Additionally, emergency drug doses should be calculated and drawn up in labeled syringes or vials prior to beginning the anesthetic procedures. Attempting to calculate, draw up, and administer emergency drugs for a 50-g (1.8-oz) ermine can be problematic at the time of an anesthetic emergency. Drug dosages used are extrapolated from the dog or cat unless specific doses are available for species such as the ferret (Carpenter, 2005).

BIOLOGY

Mustelidae

Mustelids are members of the order Carnivora, which contains six additional families. There are 67 species of

mutelids in 27 genera that include the wolverine, fisher, nearctic otter, sea otter, polecat, marten, ferret, badger, tayra, grison, and skunk. Mustelids are distributed in all continents except Antarctica and Australia. The otters have the widest distribution, being found in North, Central, and South America as well as in Africa, Europe, and Asia. Mustelid habitats range from Arctic tundra to tropical rain forest and they are terrestrial, arboreal, fossorial, and found on the open seas, as with the sea otter. Many are small (less than l kg or 2.2 lb), whereas some are relatively large (45 kg or 99 lb) when compared with members of other mammalian families. The smallest, the weasel, rarely exceeds 19 cm (7.5 in) in length. The giant river otter is the longest mustelid reaching a length of up to 190 cm (6.2 ft). Most are carnivorous (otter and fisher) but some are omnivorous (skunk). All have five toes on each foot with non-retractable claws. Sexual dimorphism is marked in most mustelids but is less apparent in badgers, otters and skunks. Male skull size may range from 5% to 25% longer than that of females. Mustelids possess prominent sharp canines, cutting carnassials, heavy premolars, and powerful jaws that are capable of crushing thick bones. The dental formula varies within and between subfamilies. As examples the European common weasel has the dental formula of I 3/3, C 1/1, P 3/3, M 1/2 = 36, whereas the dental formula of the wolverine is I 3/3, C 1/1, P 4/4, M 1/2 = 36. Mustelids lack both a clavicle and an appendix. The otters, like other aquatic carnivores, have a multilobulated (reniculated) kidney (Baitchman and Kollias, 2000). The renal lobules are firmly compressed against each other, forming a somewhat solid kidney. Musk is present in most species and produced by modified sebaceous glands present and stored in perianal sacs. The composition of musk varies among species and is used for demarcation of territory often for generations. In the case of skunks, musk is used for defense purposes. The reproductive biology of mustelids also varies among species, with males and females of most species living separately the majority of the year. Mustelids are induced ovulators and require vigorous copulation for ovulation. Males have a baculum (os penis) and females an os clitoris. Delayed implantation, up to 10 months, is exhibited in 16/67 mustelid species. The mediators of delayed implantation are largely unknown and may include environmental factors such as photoperiod. Delayed implantation can occur in semidormancy.

Procyonidae

The Procyonidae are small to medium-sized, long-bodied, and long-tailed mammals in the order Carnivora. There are 16 New World species, including the raccoon, white-



Figure 36.1. Large procyonids and mustelids are restrained in squeeze cages to facilitate intramuscular injection of parenteral anesthetic drugs.

nosed coati, and kinkajou. New World procyonids inhabit temperate, tropical, and neotropical regions. Procyonids are generally omnivores but are known to be opportunistic carnivores. The dental formula is I 3/3, C 1/1, P 4/4, M2/2 = 40. An exception to this formula is the kinkajou, which has P3/3. The molars of all procyonids are large and well adapted to crushing. There is some interspecies variation in dentition, which relates to food preferences. Subsequently procyonids have highly specialized gastrointestinal systems with all



Figure 36.2. A transport cage for a North American river otter (Lutra canadensis). Note the solid wood sides to reduce visual stimulation and prevent damage to the teeth and feet that can occur when confined to a wire cage. A clear door allows inspection of the animal during transport.

Table 36.1. General procyonidae chemical restraint agent doses (IM).

Agent(s) and Dose(s)	Reversal Agent	Comments
Ketamine (10–30 mg/kg ^a)	None	High end of dose range used for smaller animals
Ketamine $(10 \text{ mg/kg}) + \text{Diazepam}$ (0.5 mg/kg^a)		Minimal respiratory depression
Ketamine (10 mg/kg) + Midazolam (0.25-0.5 mg/kg ^a)		Minimal respiratory depression
Ketamine $(10 \text{ mg/kg}) + \text{Xylazine}$ $(1-2\text{mg/kg}^{b})$		Good muscle relaxation
Ketamine (2.0–5.0 mg/kg) + Medetomidine (0.025–0.05 mg/kg ^c)	Antipamezole (0.1 mg/kg) Ketamine: none	
Ketamine (5–15 mg/kg) + Xylazine (1–2 mg/kg) + Atropine (0.04 mg/kg ^d)	Actualistic Horic	Induction: 3–5 min Anesthesia: 15–20 min Recovery: 60–90 min
Tiletamine/Zolazepam (10–25 mg/kg ^a)	Tiletamine: none Zolazepam:Flumazenil	Chemical capture and minor surgery
Tiletamine/Zolazepam (3–5 mg/kg ^e)	Tiletamine: none Zolazepam:Flumazenil	

^aLabate AS, Nunes ALV, Gomes M, et al. Order Carnivora, Family Procyonidae (Raccoons, Kinkajous). In: Fowler ME, Cubas ZS, eds. *Biology, Medicine, and Surgery of South American Wild Animals*. Ames, IA: Iowa State University Press, 2001:317–322.

^bNielsen L. Chemical Immobilization of Wild and Exotic Animals. Ames, IA: Iowa State University Press, 1990.

^cJalanka HH, Roeken BO. The use of medetomidine, medetomidine-ketamine combinations, and atipamezole in non-domestic mammals: a review. *J Zoo Wildl Med* 1990;21:259–282.

^dMehren KG. Procyonidae. In: Fowler ME, ed. *Zoo and Wild Animal Medicine*. Philadelphia: W.B. Saunders, 1986:816–820.

^eDenver M. 2000. Procyonidae and Viveridae. In: Fowler ME, Miller RE, eds. *Zoo and Wild Animal Medicine*. Philadelphia: W.B. Saunders, 2000:516–523.

Table 36.2. Specific Procyonidae chemical restraint agent doses (IM).

Adult Weight Range (kg)	Agents and Doses (mg/kg)	Reversal Agent (mg/kg)	Comments
Coatimundi (Nausa spp.)			
3-6	Ketamine (20) + Xylazine $(1)^a$	None reported	
3-13	$\begin{array}{c} \text{Medetomidine} \ (0.0510.064) \ + \\ \text{Ketamine} \ (2.57.7) \ + \\ \text{Butorphanol} \ (0.340.36)^b \end{array}$	Atipamezole (0.25) (1/2 SC; 1/2	IM) Prolonged recovery in some cases with higher ketamine doses
Olingo (Bassaricyon gabbii)			
0.9–1.5	Tiletamine/Zolazepam (5) ^a		Supplement with Ketamine (5)
Raccoon (Procyon lotor)			
2–12	Ketamine (20) + Xylazine $(4)^c$	Yohimbine (0.15)	
	Tiletamine/Zolazepam (12) ^c		Alternatives
	Ketamine (20) + Acepromazine (0.1) ^c		
	Tiletamine/Zolazepam (3) + Xylazine (2) ^d		60 min handling time; 120 min to full recovery
Kinkajou (Potus flavas)			
1.4-4.6	Ketamine (5.5) + Medetomidine (0.1) ^e	Atipamezole (0.5)	Wild/Free-ranging kinkajous
	Ketamine (25) ^c		Alternative choice
	Tiletamine/Zolazepam (10) ^d		Alternative choice
Ringtail (Bassariscus astutus)			
0.8-1.3	Tiletamine/Zolazepam (10) ^a		
	Ketamine (10) + Acepromazine $(0.2)^{f}$		Alternative choice

^aSeal US, Kreeger TJ. Chemical immobilization of furbearers. In: Novak M, Baker JA, Obbard ME, et al., eds. *Wild Furbearer Management and Conservation in North America*. Toronto: Ontario Ministry of Natural Resources, 1987:191–215.

Table 36.3. General mustelid chemical restraint agent doses (IM).

Agents and Doses (mg/kg)	Reversal Agent (mg/kg)	Comments
Ketamine (10) + Xylazine $(1-2)^a$	Xylazine:Yohimbine (0.125) or Antipamezole (0.02–0.06)	
Ketamine (10–15) ^a	None	
Tiletamine/Zolazepam (3-6) ^a	None	
Ketamine (10–40) ^b	None	Immobilization
Ketamine (20) + Xylazine (2) ^b	Xylazine: same as above	Immobilization
Tiletamine/Zolazepam (1.5–10) ^b	None	Higher end of dosage range may produce prolonged recovery
Ketamine (22) + Diazepam $(0.4)^b$	None given	
Tiletamine/Zolazepam (2.2–22) ^c	Zolazepam:Flumazenil (0.05-0.10)	Reported for numerous species of mustelids

^aFowler ME, ed. Restraint and Handling of Wild and Domestic Animals, 2nd ed. Ames, IA: Iowa State University Press.

^bGeoroff TA, Boon DA, Hammond EE, et al. Preliminary results of medetomidine-ketamine-butorphanol for anesthetic management of captive white-nosed coati (*Nasua narica*). *Proc Amer Assoc Zoo Vet* 2004;388–391.

^cKreeger JJ, Arnemo JM, Raath JP. Handbook of Wildlife Chemical Immobilization. Fort Collins, CO: Wildlife Pharmaceuticals, 2002.

^dBelant JL. Field Immobilization of Raccoons (*Procyon lotor*) with Telazol and Xylazine. *J Wildl Dis* 2004;40:787–791.

^eFournier P, Fournier-Chambrillon C, Vie J-C. Immobilization of wild kinkajous (*Potos flavus*) with medetomidine-ketimine and reversal by atipamezole. *J Zoo Wildl Med* 1998;29:190–194.

^fJessup DA. Restraint and chemical immobilization of carnivores and furbearers. In: Nielsen L, Haigh JC, Fowler ME, eds. *Chemical Immobilization of North American Wildlife*. Milwaukee: Wisconson Human Society, 1982:227–244.

^bPimentel TL, Reis ML, Passerino AS. Order Carnivora, Family Mustelidae. In: Fowler ME, ed. *Biology, Medicine and Surgery of South American Wild Animals*. Ames, IA: Iowa State University Press, 2001:323–331.

^cFernandez-Moran J. Mustelidae. In: Fowler ME, Miller RE, eds. *Zoo and Wild Animal Medicine*. Philadelphia: W.B. Saunders, 1999:505–516.

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Table 36.4.

Adult Weight Range (kg)	Agents and Doses (mg/kg)	Reversal Agent (mg/kg)	Comments
Badger, Euro	Badger, European (Meles meles)		
5.5–12.5	Ketamine $(20)^a$	None	Recovery considered prolonged; \bar{x} hr = 170 bpm
$\bar{\mathbf{x}} = 9.3$	Ketamine (15) + Midazolam $(0.4)^a$	None given	Few advantages over ketamine alone; \bar{x} hr = 150 bpm
	Ketamine (10) + Midazolam (1.0) ^a	None given	Few advantages over ketamine alone; $x \text{ hr} = 160 \text{ bpm}$
	Ketamine (5) + Medetomidine (0.080)	Medetomidine: Atipamezole (0.80)	Best quality of maintenance; lower mean HR than other agents used $(\vec{v} = 100 \text{ hrm}) \cdot \vec{v}$ arterial blood
			pressure = 150 mmHg was higher than other agents
			excitement
	Ketamine $(5-10)$ + Medetomidine $(0.05-0.10)^b$		Preferred combination
	Tiletamine/Zolazepam (2.5) + Medetomidine $(0.04)^{0}$	Medetomidine: Atipamezole (0.20)	Alternative combination
10-16	Tiletamine + Zolazepam $(10)^{c}$		Supplement with Ketamine (5 mg/kg)
	Netainine (13) + Acepioniazine (0.4) Ketamine (16) + Xvlazine (6) ^c		
n = 93	Medetomidine (0.02) + Ketamine	None given	Induction slower than ketamine, but quality of
5.5-12.5	$(0.04) + Butorphanol (0.08)^d$		induction similar (range = $3-22 \text{ min } \bar{x} = 6 \text{ min}$);
			paler mucous membranes than ketamine alone; recovery 37–39 mins; sudden arousal or recovery
			occurred in 14/93 (15%) of the badgers using these combinations and was statistically linked to
			increasing rectal temperature
	Medetomidine (0.02) + Ketamine	None given	
	$(0.04) \pm 0$ until pitatrot $(0.00)^{-1}$	None given	
	(0.06) + Butorphanol $(0.04)^d$	IVOITE BIVEII	
Badger, Chino 1–3	Badger, Chinese Ferret (<i>Melogale moschata</i>) $1-3$ Tiletamine/Zolazepam (5) ^c		Supplement with ketamine (5 mg/kg)
Badger, Hog (Badger, Hog (Arctonyx collaris)		Cumplement with Letenning (2.2 mg/lrs)
1-1 1	metannine/201azepann (±.±)		Supplement with retaining (2.2 mg/ng)
Badger, Hone 7-13	Badger, Honey (Ratel) (<i>Mellivora capensis</i>) 7–13 Tiletamine/Zolazepam $(2.2)^e$ Ketamine $(6) + Xylazine (0.5)^e$		Supplement with ketamine (2.2 mg/kg)
Badger, Amer 4–12	Badger, American (<i>Taxidea taxus</i>) 4-12 Tiletamine/Zolazepam (4.4) ^f		Supplement with ketamine (4.4 mg/kg)
	Ketamine (15) + Xylazine (1) ¹		Alternative choice
Ermine (<i>Mustela erminea</i>) 0.05-0.365 Ketamine (Tiletamine	tela erminea) Ketamine (5) + Medetomidine (0.0001 mg/gm) $(0.1)^c$ Tiletamine/Zolazepam (0.011-0.022 mg/gm) $(11-22)^b$	Atipamezole (0.0005 mg/gm)(0.5); $1/2 \text{ IV} + 1/2 \text{ IM}$	Supplement with ketamine (2.5 mg/kg)
Black-Footed 0.7-1.5	Black-Footed Ferret (<i>Mustela nigripes</i>) 0.7–1.5 Ketamine (3) + Medetomidine $(0.075)^b$ Ketamine (35) + Diazepam (0.2)	Medetomidine: Atipamezole (0.375); $1/2 \text{ IV} + 1/2 \text{ IM}$	
Ferret (Mustela putorius) 0.6-1.2 Ketamine Retamine	Ia putorius) Ketamine (25) + Xylazine (2) ^c Ketamine (25) + Acepromazine (1.1) ^c		Supplement with ketamine (12 mg/kg)

	Tiletamine/Zolazepam (15) ^c Ketamine (5) + Medetomidine (0.1) Ketamine (10–30) + Xylazine (1–2) or Diazepam	Medetomidine: Atipamezole (0.50)	Recovery may be prolonged
	Ketamine (25–35) + Diazepam (2–35) Ketamine (25–35) + Diazepam (2–3)8 Medetomidine (0.08) + Butorphanol (0.1)8 Ketamine (5) + Medetomidine (0.08) ^h Ketamine (5) + Medetomidine (0.08) +	Medetomidine: Atipamezole (0.40) Medetomidine: Atipamezole (0.40) +	Anesthesia; poor analgesia Anesthesia; monitor blood pressure and ventilation Induction for inhalation anesthesia Induction for inhalation anesthesia
	Butorphanol $(0.1)^{11}$ Ketamine $(5-10) + \text{Midazolam} (0.25-0.50)^{\text{h}}$ Propofol $(5-8 \text{ IV})^{\text{i}}$	butorpnanoi:Naloxone (U.UL-U.U4) None	Induction for inhalation anesthesia Anesthesia induction
	Diazepain (U.S-5-0.9 SC of IN) F Butorphanol (0.1–0.5 SC, IM, IV) i Buprenorphine (0.01–0.03 SC, IM, IV) i	Naloxone (0.01–0.04) Naloxone (0.01–0.04)	r enreuteation Premedication analgesia Premedication analgesia
	Oxymorphone (0.05–0.2 SC, IM, IV) ⁱ Morphine (0.2–2.0 SC, IM) ⁱ	Naloxone (0.01–0.04) Naloxone (0.01–0.04)	Premedication analgesia Premedication analgesia
	Meperiaine $(9-10.3C, 1M)^{\circ}$ Atropine $(0.02-0.05)^{i}$	natoxone (0.01-0.04) None	Premedication analgesia Premedication to maintain heart rate and
	Glycopyrrolate (0.01) ⁱ	None	Premedication to maintain heart rate and derrease serretions
	Acepromazine (0.1) + Butorphanol (0.2) +	Butorphanol: Naloxone (0.01–0.04)	Premedication, moderate to deep sedation
	Midacontroller (0.1) + Oxymorphone (0.1) + Oxymorphone (0.1) +	Oxymorphone: Naloxone (0.01–0.04)	Premedication, moderate to deep sedation
	Acepromazine (0.05) + Butorphanol (0.1) + Ketamine (10) ⁱ	Butorphanol: Naloxone (0.01–0.04)	Premedication, moderate to deep sedation
Ferret, European Male $(n = 11)$ 0.84-1.04 Female $(n = 1)$ 0.64	Ferret, European or Polecat (Mustela putorius) Male $(n=11)$ Ketamine (10) + Medetomidine $(0.20)^{\rm i}$ $0.84-1.04$ Female $(n=1)$ 0.64	Medetomidine: Atipamezole (1.0 IM) injected 28.1-54.0 min after ket/med injection, standing in 1.5-9.4 min; ambulatory in 10.0-25.7 min	Free-ranging polecats; captured for clinical examination; blood collection and placement of intraabdominal radio transmitters; induction smooth and rapid (0.7–3.9 min); degree of anesthesia and muscle relaxation satisfactory in most individuals; all animals exhibited decreased heart rate, respiratory rate, and temperature; hypothermia was significant and was controlled/prevented by placing animals on a warmed plastic table (37°C).
Fisher (Martes pennanti) 2.6–5.5 Ketamin	$\begin{tabular}{ll} $$\operatorname{Fermion}(2)$ \\ $\operatorname{Tiletamine}(2)$ \\ $\operatorname{Ketamine}(3)^k$ \\ $\operatorname{Ketamine}(3)^k$ \\ \end{tabular}$	None used Xvlazine: Atipamezole (0.02–0.06 1/2 IM, 1/2 SC)	Wild caught/trapped Wild caught/trapped: High dose range
4.7–5.8 (Males) 2.3–2.9 (Females)	$\label{eq:Ketamine} \begin{aligned} & \text{Ketamine } (3.24.2) + \text{Medetomidine } (0.0620.078)^I \\ & \text{Ketamine } (3.33.9) + \text{Medetomidine } (0.0630.077)^I \end{aligned}$	after 45 min immobilization None given None given	Recently wild caught; \bar{x} induction time = 4.6 min; \bar{x} down time = 147 min; \bar{x} alert time = 147 min;
4.7-5.8 (Males)	Ketamine (16.9–20.5) ^c	None	\bar{x} recovery time = 200 min; mild bradycardia and hypertension; calm recovery; temp = 38°C-40°C
	Ketamine (17.0-21.4) ^c	None	Recently wild caught; \bar{x} induction time = 4.5 min; \bar{x} down time = 36 min; \bar{x} alert time = 41 min; \bar{x} recovery time = 81 min; increased muscle tone and labored respiration temperature = 38.9-40.3°C.
2.6–5.5	Ketamine (20) + Medetomidine $(0.040)^c$ Ketamine (20) + Acepromazine $(0.10)^c$	Medetomidine: Atipamezole (0.02) None	Supplement with Ketamine (10)

Table 36.4. (C	(Continued)		
Adult Weight Range (kg)	Agents and Doses (mg/kg)	Reversal Agent (mg/kg)	Comments
Marten (<i>Marte</i> 0.5-1.5	Marten (Martes americanus) $0.5-1.5$ Ketamine $(10) + Medetomidine (0.2)^c$	Medetomidine: Atipamezole (1; 1/2 IM, 1/2 SC)	Prone to hyperthermia; supplement with ketamine
	$Ketamine (18) + Xylazine (1.6)^c$	Xylazine: Antipamezole (0.02–0.06) or Yohimbine (0.2–0.5) IM	(5 mg/kg) IM II maicated
Mink, America 1.13–1.81 $\bar{x} = 1.51$ (Males or Females)	Mink, American (Mustela vison) 1.13–1.81 Ketamine (22.1–24.8) + $\bar{\mathbf{x}}$ = 23.2 $\bar{\mathbf{x}}$ = 1.51 (Males or Females)	None	Ranch raised and bred adults ($n = 22$); time to immobilization (lateral recumbency with no purposeful movements) = 2–4 min; time to anesthesia (no movement in response to [unspecified] pain) = 5–10 min; time to recovery (period from initial injection until mink could
0.8-1.1	Tiletamine/Zolazepam (15) $^{\mathrm{c}}$	None specified	stand unaided) = 60 min; muscle relaxation improved over 60 min period of immobilization Supplement with Ketamine IM (15 mg/kg) if
	Ketamine (5) + Medetomidine $(0.1)^c$ Ketamine (40) + Xylazine $(1)^c$	Atipamezole (5), 1/2 IM, 1/2 SC Xylazine: as above for Marten	appropriate Alternative Alternative
Mink, Europea Males $(n = 6)$ 0.77–1.03 Females $(n = 8)$ 0.42–0.54	Mink, European (<i>Mustela lutreola</i>) Males $(n = 6)$ Ketamine (10) + Medetomidine $(0.20)^{j}$ 0.77 – 1.03 Females $(n = 8)$ 0.42 – 0.54	Medetomidine: Atipamezone (1.0) IM injected 28.1–54.0 min after ket/med injection; standing in 1.5–9.4 min; ambulatory in 10–25.7 mins	Free-ranging mink captured for clinical examination, blood collection and placement of intraabdominal radio transmitters. Induction smooth and rapid (0.7–3.9 min); degree of anesthesia and muscle relaxation satisfactory in most individuals; all animals exhibited decreased heart rate and respiratory rate, and rectal temperature. Hypothermia was significant and was controlled/prevented by placing animals on a warmed plastic table (37°C)
Otter (America Males 2.90–9.30 $\bar{x} = 5.64$ Females 3.6–8.0 $\bar{x} = 5.50$	Males 2.90–9.30 Ketamine (15) + Midazolam (0.3) or Diazepam $\bar{x} = 5.64$ (0.5) (Male and Female > 4.5 kg) ⁿ Females 3.6–8.0 Ketamine (20) + Midazolam (0.30) or Diazepam $\bar{x} = 5.50$ (0.5) (Male and Female < 4.5 kg) ⁿ	None Used	Wild–caught otters immobilized 1–5 days post-capture. Conditions of immobilization: Restrained in portable squeeze cage, which was covered with a drape to block light and injected IM. Room lights out and no sound stimulation. Induction reached (lateral decumbency and no response to touch) in 10–12 min. Immobilization time: 30–45 min. Procedures (physical examination, wound care, bandaging, and blood collection) sometimes required administration of one additional 20–30 mg dose of ketamine HCl IV or isoflurane (0.5%–1%) via face mask. This provided an additional 20 min. working time. If procedures extended beyond this 20 min. time frame, the otters were intubated, maintained on isoflurane (0.5%–1.5%), and given

			intermittent positive pressure ventilation every 15 seconds if they were hypoventilating. Monitoring included HR (range = 120–264 bpm; mean = 166), RR (range = 12–56/min; mean = 30/min) and rectal temperature (range = 99.80°F-104.7°F; mean = 101.8°F). Otters were recovered in their holding cage (room temp = 60°F), which was padded with towels and the front draped with a sheet to decrease light and sound stimulation. Complete recovery times (normal ambulation and mentation) ranged from 30–90 min. Hyperthermia may be an issue if otters become hyperactive during recovery. If this occurs, sedation and other corrective measure may be necessary (midazolam IM, placing a fan directed through the cage cars, decreasing ambient temperature). No mortalities, and few complications, occurred using this protocol in over
Males and Female combined (free-ranging):	Males and Females Ketamine (10) + Midazolam (0.25)° combined Ketamine (2.5) + Medetomidine (0.025)° (free-ranging):	None given Medetomidine: Atipamezole (0.125)	250 immobilizations and anesthetic episodes. Highly recommended Avoid in hypothermic otters. May need higher doses (Ket 3.5 + Med 0.035 mg/kg) but respiratory
geographic locations (males may be 17%	Titelamine/Zolazepam (4–8)° Ketamine (10) Ketamine (10) + Diazepam (0.5–1.0)°	Zolazepam:Flumazenil (0.08) IM None None given	Recovery may be prolonged without Flumazenil Expect muscle rigidity and variable duration Prolonged recovery compared to Ketamine +
females); Males and females combined	Ketamine $(5-10)$ + Xylazine $(1-2)^{\circ}$	Xylazine:Yohimbine (0.125)	Variable effects from heavy sedation to immobilization. May get respiratory depression.
(captive) 5.7-13	Azaperone $(0.1) + Fentanyl (0.1-0.2)^0$	Fentanyl:Naloxone (0.04)	Not recommended. Reports of fatal complications.
Otter, Asian Sm 1-5	Otter, Asian Small-Clawed (Aonyx cinerea) 1–5 Ketamine (15–18) + Midazolam $(0.75-1.0)^{\rm b}$ Ketamine $(4–5)$ + Medetomidine $(0.10-0.12)^{\rm b}$	Medetomidine: Atipamezole (0.50–0.60) IM	Respiratory depression may occur. Avoid in cold
	Tiletamine/Zolazepam (6–9)°	Zolazepam: Flumazenil (0.08) IM	епунопшенкэ—пуропенша.
Otter, Clawless 10–12	Otter, Clawless (Aonyx capensis) $10-12 \hspace{1cm} Tiletamine/Zolazepam (5)^{c} \\ Ketamine (8) + Xylazine (1)^{c}$	None given Xylazine: Yohimbine (0.125 IV)	Supplement with Ketamine 2.5 mg/kg IM
Otter, Sea (Enhydra Iutris) Males 22–45 Butorphan Females 15–32 Diazepam (<i>ydra lutris)</i> Butorphanol (0.5) or Oxymorphone $(0.3)^b$ Diazepam (0.5) + Oxymorphone $(0.3)^p$	Naloxone (0.04) IV or IM	Sedation to immobilization Sedation for intubation and subsequent inhalation
	Fentanyl (0.1 \pm 0.003) + Diazepam (0.1 \pm 0.006) ^{P.Q} n = 294	None used	Wild otters involved in oil spill rehabilitation; lighter sedation and shorter-acting than when either
	Fentanyl (0.1 ± 0.02) + Azaperone (0.5 ± 0.02) + Diazepam (0.3 ± 0.01) ^{p.q} n = 61 Fentanyl (0.1 ± 0.006) + Acepromazine (0.14 ± 0.01) + Diazepam (0.2 ± 0.01) ^{p.q} n = 32	None used	aceptonazine of azaperone was auteu. Deeper sedation than Fentanyl/Diazepam and duration up to 2.5 h

Adult Weight Range (kg)	Agents and Doses (mg/kg)	Reversal Agent (mg/kg)	Comments
	Meperidine (13 \pm 0.5)+ Diazepam (0.2 \pm 0.01) p,q	None used	A higher mortality rate occurred in this group
Males $n = 230$ $\overline{x} = 25.6$	For surgical procedures Fentanyl (0.33) + Diazenam (0.11) ^r	Fentanyl: Naltrexone administered at $2\times$ the total Fentanyl dose (1/2 IV. 1/2 IM)	Free-ranging of the n in n
Females $n = 367$ $\bar{x} = 21.1$			instrumentation; smooth induction with minimal need for supplemental anesthesia during procedures lasting 30-40 min. Only 1 anesthesia
			related mortality (0.2%); reversal with Naltrexone occurred in 1–3 minutes. No opioid recycling was observed.
	For nonsurgical biological sample collection procedures Fentanyl (0.22) + Diazepam (0.07) ^r	Same as above	
Otter (Europea 1 3-14	Otter (European) Eurasian (<i>Lutra lutra</i>) 3-14 Ketamine (18) + Diazepam (0.4) ⁵ Ketamine (15) + Diazepam (0.5) ^b Ketamine (15) + Diazepam (0.5) ^b	None given	May cause respiratory depression
n = 38 Males (13) and Females (25) Range (Males	Keramine (5) + Medetomidine (0.05) ¹⁷ Ketamine (4.3–5.9) $\bar{\mathbf{x}} = 5.1$ + Medetomidine 5) $(0.043-0.059) \bar{\mathbf{x}} = 0.051 (82 \text{immobilizations})$ in 38 animals) ^b	Medetomidine: Atipamezole (0.2.5) IM Medetomidine: Atipamezole (0.22–0.30) 5 x IM Medetomidine dose given 30–40 mins post- induction. Animals were able to move and respond to external stimuli in <5 mins Mild	Avoid using in cold environments, hypothermia Recently captured free ranging otters mean initial effects in 3 min mean induction time = 5.5 min. (hr = 95 bpm.) mean resp rate = 32 bpm. Relative O. saturation = 93% (recal temp = 38.4°C)
$\frac{3-8.7}{\overline{X}} = 5.3$		ataxia noted in a few animals 5 hrs post Atipamezole.	
Otter, Spotted-N Average 4	Otter, Spotted-Necked (<i>Lutra maculicollis</i>) Average 4 Tiletamine/Zolazepam (5) $^{\rm e}$	None given	Free-ranging otters supplement with Ketamine
	Ketamine $(5-8)$ + Xylazine $(0.5-1.0)^e$	None given	(5 mg/kg) Alternative drugs
Skunk, Hog-Nos 2.3–4.5	Skunk, Hog-Nosed (Conepatus leuconotus) 2.3–4.5 Tiletamine/Zolazepam $(10)^{t}$ Ketamine $(15) + Acepromazine (0.2)^{t}$	None given None given	Supplement with Ketamine (10) Alternative drugs
Skunk, Hooded 0.7-2.5	Skunk, Hooded (<i>Mephitis macroura</i>) 0.7–2.5 As above	As above	As above
Skunk, Striped 2-3	Skunk, Striped (<i>Mephitis mephitis</i>) 2–3 Tiletamine/Zolazepam (10) ^u	None given	Field immobilization of free ranging skunks.
Kits 0.8–1.9 mean = 1.2 $(n = 78)$	Ketamine $(36.3-62.0)^m 0 = 52.4$	None	Field immobilization: scent gland removal; immobilization time = 1–3 min; surgical anesthesia = 10–15 min; recovery = 60–90 min.
Kits 0.5–1.8 mean = 1.0 $(n = 43)$	Ketamine $(32.9-69.0)^{m} 0=36.8$	None	I mortality due to aspiration. Field immobilization: scent gland removal; immobilization time = 2-4 min; surgical anesthesia = 5-10 min; recovery = 45-74 min

 Table 36.4.
 (Continued)

Field immobilization: scent gland removal; immobilization = 1–4 min; surgical anesthesia = 35–90 min; recovery = 60–120 min. Better muscle relaxation than above two groups.	•	Captive	See above	If not immobilized in 15 minutes, repeat full dose (decrease dose by 1/2 in captive wolverines) Alternative drugs
None	None	None given	See above	None Medetomidine: Atipamezole (0.5–0.45) Medetomidine: Atipamezole (1.5, 1/2 IV, 1/2 IM) None Etorphine: Diprenorphine (0.2 mg/kg); Xylazine: Yohimbine (0.15 mg/kg)
-2.5 Ketamine $(39.2-107.7)^{m}$ mean = 7.3 $1 = 1.1$	Ketamine (15) + Acepromazine $(0.2)^b$	Tayra (<i>Eira barbata</i>) 4-6 Tiletamine/Zolazepam (3.3) ^b	Weasel, Long Tailed (Mustela frenata) 85–200 grams See above (Ermine)	Wolverine (<i>Gulogulo</i>) Ketamine (20) + Acepromazine (0.2) ^b Ketamine (5-8) + Medetomidine (0.1-0.15) Ketamine (7) + Medetomidine (0.3) ^c Ketamine (20) + Acepromazine (0.2) ^c Etorphine (0.1) + Xylazine (1) ^c
Kits 0.6–2.5 mean = 1.1		Tayra (E 4-6	Weasel, Long 85–200 grams	Wolveri

Pernandez-Moran J, Perez E, Sanmartin M, et al. Reversible immobilization of Eurasia otters with a combination of ketamine and medetomidine. J Wildl Dis 2001;37:561–565. ^aThornton PD, Newman C, Johnson PJ, et al. Preliminary comparison of four anesthetic techniques in badgers (*Meles meles*). Vet Anesth Analg 2005;32:40–47.

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^eMcKenzie AA, Burroughs REJ. Chemical capture of carnivores. In: McKenzie AA, ed. The Capture and Care Manual. Pretoria: Wildlife Decision Support Services and the South African Veterinary Foundation, 1993:224–243.

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⁸Carpenter JW, ed. *Exotic Animal Formulary*. Philadelphia: Elsevier Saunders, 2005.

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*Witcheltree DH, Serfass TL, Tzilkowski WM, et al. Physiological responses of fishers to immobilization with ketamine-xylazine or Telazol. Wildl Soc Bull 1999;27:582–591.

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mRamsden RO, Coppin PE, Johnson DH. Clinical observations on the use of ketamine hydrochloride in wild carnivores. J Wildl Dis 1976;12:221-2?

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Monson DH, McCormick C, Ballachey BE. Chemical anesthesia of northern sea otters (Enhydra lutris): results of past field studies. J Zoo Wildl Med 2001;32:181–189

³ Kulken T. Anaesthesia in the European otter (*Lutra lutra*). Vet Rec 1998;123:59.

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'Seal US, Kreeger TJ. Chemical immobilization of furbearers. In: Novak M, Baker JA, Obbard ME, et al., eds. Wild Furbearer Management and Conservation in North America. Toronto: Ontario Ministry of Natural Resources, 1987:191–215.

^uLariviére SL. Immobilization of striped skunks with Telazol. Wildl Soc Bull 1996;24:713-716.

members of the family lacking a cecum. The feet of procyonids have five toes and they walk partly or wholly on the soles of their feet (plantigrade). Claws are non-retractable, except the ringtails, which have semi-retractable claws on their front feet. All procyonids have agile front feet, which make them excellent climbers. Except for the coati, procyonids are generally nocturnal or crepuscular. Females usually breed in the spring of their first year and males from their second year on. The small procyonids live 10 to 15 years in captivity. The authors are aware of a male kinkajou that lived to 32 years of age in a zoo, although in the wild it is unusual for procyonids to exceed 7 years of age.

CHEMICAL RESTRAINT, IMMOBILIZATION, AND ANESTHESIA

Delivery of injectable agents to procyonids and mustelids, as with other wild mammals, often requires physical restraint and specialized supplies and equipment (see Chapters 4 and 12). Squeeze cages or boxes and transfer boxes (Figures 36.1 and 36.2) greatly facilitate delivery of injectable drugs and help to minimize stress (see Chapter 9), while maximizing the quality of induction, immobilization, and recovery of procyonids and mustelids. As an example, when recently captured nearctic river otters (Lontra canadensis) are transferred from their holding cages to a small squeeze cage, injected, and the squeeze cage is then covered with a drape or towel and minimal environmental noise occurs, the otters are consistently immobilized in 10 to 12 minutes and remain so for 35 to 45 minutes. If this protocol is not consistently adhered to otters never reach an acceptable level of immobilization. Complications such as hyperthermia occur because of excessive movement, and recovery is unacceptable because of hyperkinesis vocalization and disorientation (Kollias, 1999). Numerous general and specific single drugs or drug combinations have been reported for chemical restraint, immobilization, and anesthesia of procyonids (Tables 36.1 and 36.2) and mustelids (Tables 36.3 and 36.4). In the authors' experiences the doses listed are guidelines for use and often require modification when applied to specific individuals or collections of animals and whether they are used for captive, recently captured, or free-ranging procyonids or mustelids.

INHALATION ANESTHESIA

Generally, induction of inhalation anesthesia is facilitated by prior administration of injectable agents recommended in Tables 36.1, 36.2, 36.3, and 36.4 and in standard veterinary anesthesia texts for domestic dogs and cats (Seymour and Gleed, 1999; Muir and Hubbell, 2007). The polecat and ferret are mustelid species for which a number of injectable and inhalation anesthesia protocols have been published (Tables 36.3 and 36.4;

Gaynor et al., 1997; Evans and Springsteen, 1998; Imai et al., 1999; Cantwell, 2001; MacPhail et al., 2004; Vastenburg et al., 2004). Isoflurane and sevoflurane have been shown to be safe and efficacious and are agents of choice in both procyonids and mustelids (Schumacher, 1996; Gaynor et al., 1997; Denver, 2000). Following administration of preanesthetic agents or parenteral drugs some animals may still require restraint. They can be held in a towel or with gloves and provided the inhalant agent via face mask or induction chamber. Once the animal loses its righting reflex it is masked until it is intubated or maintained on a face mask. With intubation or face mask maintenance, inhalants should be administered using a nonrebreathing circuit (Ayre's T-piece or Bain System). Oxygen flow should be two to three times the minute ventilation (approximately 200–350 ml/kg per minute) (Cantwell, 2001). Anesthesia monitoring, thermoregulation, and cardiopulmonary support, resuscitation, and recovery for these species are as discussed in Chapters 6, 7, and 9.

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37

Viverrids

Anneke Moresco and Scott Larsen

TAXONOMY AND BIOLOGY RELATED TO ANESTHESIA AND HANDLING

Taxonomic classification of the Viverridae varies by source, and nomenclature can be confusing because sometimes the same common name is applied to different species. This chapter follows the taxonomy detailed by the IUCN small carnivore specialist group (IUCN, 2005). There are 36 species of viverridae; their Latin names, common names, weight ranges, and longevities are given in Table 37.1.

The fossil record for Viverridae is the oldest among the families classified in the Order Carnivora. Phylogenetically, they are classified as part of the *feliformia* group and are more closely related to felids than to canids (Veron and Heard, 2000). Viverrids are small to medium-sized carnivores and their natural habitat spans southwestern Europe, southern Asia, the East Indies, and Africa, including Madagascar. They are all skilled climbers and tend to be arboreal; a few are primarily terrestrial (e.g., oriental civets) and will dig burrows, use burrows dug by other animals, or seek shelter within human-built structures (Nowak, 2005).

The ecology of many species in this group is poorly known due to their elusive habits and secretive natures. Most are nocturnal or crepuscular making observations difficult. The natural social structure is typically solitary (Kingdon, 2003); however in captivity they are likely to be housed in pairs or small groups. This needs to be taken into account during induction and recovery.

As their taxonomic classification suggests, most viverrids are carnivorous and a high percentage of their diet (70%) consists of meat (Ray and Sunquist, 2001). However, the binturong (*A. binturong*) and many civet species are more omnivorous, with up to 40% of their diet consisting of fruit. For many species, the diets in the wild are unknown because these animals are difficult to study under free-ranging conditions. Longevities have not been recorded for many viverrid species, but

documented longevities range from 10 to 30 years (Table 37.1).

ANATOMY AND PHYSIOLOGY RELATED TO ANESTHESIA

Some species have strong, sharp, retractile or semiretractile claws and many dig burrows; one should remember their raking power when physically restraining and handling these animals (Rettig and Divers, 1986). The binturong is the only viverrid with a truly prehensile tail. It is a very strong appendage and can be used with great dexterity, which should be kept in mind when handling binturongs, even when they are sedated.

As with other members of the order Carnivora, viverrids have simple stomachs and relatively short gastrointestinal tracts; in some species the cecum is absent or vestigial. In general, hind gut fermentation does not seem to be significant (Mitchell, 1905; Crapo et al., 2001) despite the large amount of fruit consumed by some species. They have correspondingly short gastrointestinal transit times. Pre-anesthetic fasting periods of 24 hours are typically appropriate; water can be withheld for 4 to 12 hours.

Mammals that consume exclusively vertebrate diets tend to have higher metabolic rates than those that also consume fruit and invertebrates (McNab, 1995). The binturong, the largest of the viverrids, does indeed have a slightly lower body temperature (37°C–38°C) than similarly sized dogs and tends to maintain normal body temperature during anesthesia (Mudappa and Chellam, 2001; Moresco and Larsen, 2003). The smaller viverrids have a larger surface-to-volume ratio, making them more susceptible to heat loss during anesthesia.

In the wild, the fanaloka (*F. fossana*) and the falanouc (*E. goudotti*) can lay down fat reserves in preparation for winter. Fat is laid down especially in the tail and may make up a significant percentage of their body weight

Table 37.1. Latin names, common names, body weights and longevity of viverrid species.

Latin Name	Common Names	Weight/Longevity ^a	Reference
Cryptoproctinae			
Cryptoprocta ferox	Fossa, Fosa	6–10 kg; ♀ 5–7 kg 7–12 kg; L:17 yr	Haltenorth and Diller, 1984
Euplerinae			
Eupleres goudotii	Small-toothed mongoose	2-4 kg	Albignac, 1974
Fossa fossana	Malagasy civet, Fanaloka,	♂ 1.8–2.7 kg,	Haltenorth and Diller, 1984
	Striped civet	♀ 1.4–1.7 kg	Nowak, 2005
		L:11 yr	
Hemigalinae			
Chrotogale owstoni	Owston's palm civet	2.5–4.0 kg	Kingdon, 2003
Cynogale bennettii	Sunda otter civet	3–5 kg	Nowak, 2005
Diplogale hosei	Hose's palm civet	Wt unk	Nowak, 2005
Hemigalus derbyanus Nandiniinae	Banded palm civet	1.75-3.0 kg	Nowak, 2005
Nandinia binotata	Two-spotted palm	1.7-3.2 kg,	Haltenorth and Diller, 1984
14didilid bilotata	civet African palm-,	♂ up to 5 kg	Traiteriottii aria Birici, 1901
	or West African	11yr	
Paradoxurinae		•	
Arctictis binturong	Binturong, Asian bear cat	14 kg, in captivity up to	Nowak, 2005; Moresco and Larsen,
3	G,	30 kg; L: 28 yr	2003; Moresco, pers. observ.
Arctogalidia trivirgata	Small toothed, three striped civet	2.0–2.5 kg	Nowak, 2005
Macrogalidia musschenbroekii	Sulawesian palm civet	3.8-4.5 kg	Nowak, 2005
Paguma larvata	Masked palm civet	3.6-5 kg	Nowak, 2005
Paradoxurus hermaphroditus	Common palm civet, musang, toddy cat		
P. jerdoni	Palm civet, musang, toddy cat, brown palm civet	1.2–3.5 kg	Mudappa and Chellam, 2001
P. zeylonensis	Golden palm civet		
Viverrinae			
Civettictis civetta	African civet	7–20 kg;	Kingdon, 2003 Haltenorth and
(Viverra civetta)		L: 14 yr	Diller, 1984
Genetta abyssinica	Ethiopian or Abyssinian genet	1.3–2 kg	Kingdon, 2003
G. angolensis	Angola or Miombo genet	1.3-2 kg	Kingdon, 2003
G. genetta	small spotted- or common genet	1.3–2.25 kg; L: 14.75 yr	Haltenorth and Diller, 1984
G. johnstoni G. maculata	Johnston's genet Pardine genet	1–3 kg 1.2–3.1 kg	Kingdon, 2003 Haltenorth and Diller, 1984
G. servalina	Servaline genet	1.2-3.1 kg 1-2 kg	Kingdon, 2003
G. thierryi	Hausa genet	1.3–1.5 kg	Kingdon, 2003
G. tigrina	Large-spotted- or rusty-	1.2–3.1 kg; L: 9.5 yr	Kingdon, 2003
	spotted genet		
G. victoriae	Giant genet	2.5–3.5 kg	Kingdon, 2003
G. cristata	genet		
Osbornictis piscivora	Aquatic genet	1.2-2.5 kg	Kingdon, 2003
Poiana richardsoni	African linsang or oyan	0.5-0.7 kg	Kingdon, 2003
Prionodon linsang P. pardicolor	Banded linsang	0.6–0.8 kg slightly smaller than	Nowak, 2005 Nowak, 2005
г. ранисон	Spotted linsang	P. linsang	NOWak, 2003
Viverra civettina	Malabar civet	5–11 kg	Nowak, 2005
V. megaspila	Large spotted civet	5–11 kg	Nowak, 2005
V. tangalunga	Malay civet	ੈ 2.45–4.3 kg;	Colon, 2002
	-	♀ 3.62–3.95 kg	
V. zibetha	Large Indian civet	5-11kg	Nowak, 2005
Viverricula indica	Lesser oriental civet, rasse	2–4 kg	Nowak, 2005

 $^{^{\}mathrm{a}}$ L = Longevity, when known, refers to captive animals.

(Garbutt, 1999); therefore, the tail is not recommended as a site for intramuscular anesthetic injection.

ANALGESIA

There is little published information on the use of analgesics in viverrids, but it is presumed that non-steroidal

anti-inflammatory drugs (NSAIDs), opioids, and local analgesics that are used in domestic cats may be similarly applied to viverrids.

A variety of NSAIDs have been used clinically in viverrids, but no studies on the safety or efficacy of these drugs have been performed. Aspirin at the domestic cat dose, 25 mg/kg q24h (Plumb, 1999) has been effective in

treating glomerulonephritis in binturongs, with no adverse effects observed clinically or as reflected in routine hematology and serum chemistry analyses up to three months after treatment (Moresco, personal observation).

Butorphanol is routinely used as an analgesic in veterinary medicine and can be incorporated into the anesthetic induction protocol (Moresco and Larsen, 2003). If no antagonist is administered, the animal can benefit from the analgesic properties of butorphanol postimmobilization; however, the duration of analgesia in cats is only about 90 minutes (Lascelles and Robertson, 2004) and is unlikely to be longer in viverrids. Additional doses of butorphanol can be administered orally, either by squirting the solution directly onto the oral mucosa or by hiding the injectable or tablet form in food items.

PHYSICAL RESTRAINT TECHNIQUES

For examination and sample collection, it is difficult to safely handle most viverrids with physical restraint techniques alone. Ultimately, the goal is to choose the restraint technique that will be the least stressful and allow the most reliable drug delivery. Recently transported animals are best left to acclimate before restraint is attempted; restraint (physical or chemical) should not be attempted if ambient temperature is above 90°F (32.2°C) (Fowler, 1986).

Net capture can be low stress and transfer out of the net may not be necessary as drugs can be delivered through the mesh. It is possible to use nets to capture animals in a tree or den in their exhibit. Nets can be used even for binturongs, the largest of the viverrids. When considering the use of nets, the importance of appropriately trained personnel cannot be over-emphasized. Animals can be transferred to a kennel after injection of anesthetics and left alone to minimize stimulation; this is particularly important when using α_2 -agonists for restraint because stressed animals can override the sedative effects of these agents. If left in the net, animals should have a cover over their eyes and noise should be minimized. There is the potential for claws getting caught in mesh; trained personnel are necessary to minimize capture time, stress, and trauma. Nets are not typically useful in free-ranging situations.

Traps or squeeze cages can be low stress if the animal has been habituated (operant conditioning) to them; transfer may not be necessary as drugs can be delivered through the mesh (may need a pole-syringe, blowpipe, or low power dart gun if trap is not a squeeze cage). If the animal is small enough, it can be transferred to a chamber for induction with inhalant anesthesia, or the entire cage can be covered with a plastic bag and inhalant anesthetics can be administered. In the field, box traps are typically used to capture small-to-medium-sized carnivores (Mudappa and Chellam, 2001; Colon, 2002). Trap success improves if traps are located near areas such

as latrines where signs of activity have been recorded. In order to habituate the animals, traps should be baited but left open for several days before setting the trap to close (Mudappa and Chellam, 2001). Many of the viverrids have nocturnal habits, so traps should be set at night and checked frequently to minimize the amount of time the animals spend inside. Checks can be less frequent if traps are equipped with devices that signal when they are triggered. Animals should spend minimal time in the traps because this can increase stress and thereby affect the quality of anesthesia, as well as increase the likelihood of self-injury. When trapping animals in the wild, keep in mind the presence of potential predators that may attack and kill the trapped animal.

Trap-related injuries may include self-mutilation, nose trauma, traumatized digits and limbs, etc. In the captive setting as well, cages can be highly stressful if the animals are not habituated to them.

Animals can be transferred from a trap to a handling (burlap) bag prior to injection, this facilitates hand injection and decreases visual stimulation. Any additional manipulation of the animal in a handling bag may increase the stress to the animal and the risk of escape or injury to the animal or personnel.

DRUG DELIVERY

Hand injection, pole syringe injection, or darting can be used to deliver anesthetic induction agents to viverrids. Darting the animal allows delivery of anesthetic drugs without physical restraint; however, there is a substantial risk of delivering the drug to the thorax or abdomen, since most viverrids are slender and relatively small. Darting is not recommended for free-ranging viverrids because they may be lost in the foliage or may fall into water before the drugs take effect. Because of their speed and agility, free-ranging viverrids would need to be darted at high speeds, which would increase the chance of fractures or other dart-induced trauma (McKenzie and Burroughs, 1993). Some authors have recommended darting larger species such as the binturong (Denver, 2003), but in our experience these animals can be safely restrained by net and hand-injected if adequate equipment and trained personnel are available for capture (Moresco and Larsen, 2003).

Small viverrid species and very young animals can be captured, manually restrained, and induced with gas anesthesia administered by face mask. Alternatively, anesthesia may also be induced by placing the animal in a chamber. Recovery times with inhalant anesthetics are usually short and minimally dependent on drug metabolism, if isoflurane or sevoflurane are used (Steffey, 1996). Mask induction is only useful in small species or young animals. Chamber induction may use large amounts of inhalant anesthetic and may result in substantial exposure of personnel to inhalant anesthetics.

The choice of restraint technique is determined by the available facilities, equipment, personnel, and the characteristics of the species, the "personality" of the individual, and to what they are habituated. In the field, it is common to trap the animals and then inject by hand or by pole syringe or blowpipe (Mudappa and Chellam, 2001). The activity of the sympathetic system and release of catecholamines can greatly impact the quality of the anesthesia, depending on the drugs used; if the animal is excited or stressed, higher dosages may be needed for drugs to be effective.

VASCULAR ACCESS SITES

In many viverrids the skin is thick, the hair is coarse, and the subcutaneous tissue is abundant (especially in obese captive animals); this makes visualization of veins difficult.

The preferred site for phlebotomy is the jugular vein because of its accessibility and the possibility of obtaining relatively large amounts of blood. The neck of viverrids tends to be cylindrical, rather than cone shaped. In binturongs the jugular vein appears to be small relative to body size and is located more lateral than it is in dogs and cats, similar to ferrets. In overweight animals, it is difficult to palpate or visualize the jugular vein unless the head of the animal is tilted somewhat below the body of the animal by extending the head and neck beyond the examination table (the head should always be supported). Before using this technique it is important to evaluate the cardiorespiratory status of the animal; arterial oxygen saturation can be monitored with a pulse oximeter. If using an anesthetic combination that includes medetomidine, veins are best visualized and accessed within 20 minutes of drug administration (Moresco and Larsen, 2003).

The cephalic vein is generally a valuable site for catheterization. In binturongs, the cephalic vein courses medially and it is often large enough to place a 20 ga (1.1 mm) \times 3/4- or 1-in. (19- or 25-mm) intravenous (IV) catheter. This vein is easily visible after clipping hair and/or moistening with isopropyl alcohol. The femoral vein is typically not visible, but can often be found adjacent to the easily palpable femoral artery. It is not recommended as the primary site of venipuncture because the artery can be punctured inadvertently, which may lead to the formation of a large hematoma. If the femoral artery is punctured, direct pressure should be applied for several minutes to minimize hematoma formation. To access the femoral vein, attempt to isolate the vein between two fingers and insert the needle perpendicular to the skin and vessel. Use a small-gauge needle [22-25 ga, 0.7-0.5 mm] to minimize vascular trauma. Some viverrids have large fat deposits in the hind leg, which may make it difficult to access the femoral artery and vein. In binturongs, the saphenous vein can be accessed on the distolateral aspect of the hind leg over the tarsus, similar to its location in dogs. It can vary considerably in size between individuals.

In some viverrids, the tail vein can be accessed for small amounts of blood but is not useful for drug administration. This vein cannot be seen or palpated. The needle is inserted medially on the ventral aspect of the tail, perpendicular to the long axis; the needle is "walked" cranially, similar to the technique in cattle. In binturongs the technique was most successful when inserting the needle about 10 cm caudal to the tail base.

ENDOTRACHEAL INTUBATION

Endotracheal intubation of viverrids is not well described in the literature; however, it is generally straightforward, as the mouth can be opened wide. In binturongs, the epiglottis is usually easily visualized and tube insertion is similar to dogs. In contrast with felids, there is minimal laryngospasm, so topical lidocaine is generally not needed. If intubation is not performed, nasal insufflation may be used for oxygen supplementation.

FIELD TECHNIQUES AND STRATEGIES

It is not recommended to dart free-ranging viverrids because this group tends to be small, fast, and elusive; they can be lost before drugs take effect and accurate dart placement is difficult. Trapping with subsequent hand injection may be the best technique for administering anesthetics in the field and has been used successfully in the common genet, the brown palm civet, and the Malay civet (Palomares, 1993; Mudappa and Chellam, 2001; Colon, 2002). Transferring the animal from the trap to a handling bag (burlap works well) and hand injecting through the bag provides a technique that is relatively safe for the animal and the handler. This technique poses some risk for injection as the target muscles cannot be directly seen; rather, the shape of the animal is seen through the bag. The animal can be left in the bag until the drugs take effect since respiration can occur through the burlap; however, it is still important to closely monitor movement and respiration during induction and recovery.

BODY WEIGHT RANGES FOR COMMONLY ENCOUNTERED SPECIES

See Table 37.1.

ANESTHETIC INDUCTION AGENTS

Anesthetic induction is often achieved with injectable drugs. The most commonly used combinations include a dissociative agent (ketamine or tiletamine) and either an $\alpha 2$ -agonist (medetomidine or xylazine) or a benzodiazepine (diazepam, midazolam, or zolazepam).

Sometimes an opioid (butorphanol) is added to further reduce the needed doses of other drugs.

The dissociative agent phencyclidine was successfully used in combination with promazine in a large number of viverrids: A. binturong, A. trivirgata, C. ferox, G. genetta, H. derbyanus, N. binotata, P. hermaphroditus, P. larvata, P. linsang, V. civetta, V. indica, and V. zibetha (Seal and Erickson, 1969). Although this drug is no longer available in the United States, the dissociative agents ketamine and tiletamine are commonly used instead. If dissociative agents are used alone, high muscle tone, persistent movement, rough inductions, and rough recoveries may occur (Seal and Ericksson, 1969). These effects have been documented with phencyclidine use in viverrids, and other dissociatives in other carnivores. Therefore the use of dissociative agents alone is not recommended. Instead, it is recommended to use a dissociative in combination with a α_2 -agonist, a benzodiazepine and/or an opioid in order to improve muscle relaxation (Table 37.2). Acepromazine has also been used in combination with ketamine in viverrids (Maddock, 1989; Fuller et al., 1990), but acepromazine has a long duration of action and is non-reversible.

The combination of ketamine-medetomidine-butorphanol has been successfully used for anesthetizing binturongs. Doses range from 2 to 8 mg/kg ketamine, 0.02 to 0.06 mg/kg medetomidine, and 0.2 to 0.5 mg/kg butorphanol; lower doses of ketamine were used with higher doses of medetomidine (Moresco and Larsen, 2003; Klaphake et al., 2005). This combination worked well in binturongs, with good inductions, stable cardiopulmonary values, and fast, reversible recoveries.

Although ketamine-medetomidine-butorphanol is recommended as an anesthetic protocol in viverrids, there may be other combinations that offer more consistent inductions while retaining reversibility.

Ketamine (6 mg/kg) has been used in combination with a relatively high dose of xylazine (10 mg/kg) in the common genet (Palomares, 1993). This combination used much lower doses of ketamine than that reported for ketamine alone (66 mg/kg) (Maddock, 1989). However, the actual doses used by Maddock varied widely, and 4 of 10 animals needed supplemental anesthetics. In brown palm civets, 15 mg/kg of ketamine and 1.5 mg/kg of xylazine achieved greater induction success (Mudappa and Chellam, 2001) (see Table 37.2).

Tiletamine-zolazepam has been recommended for several different species of viverrids, including *N. binotata, C. civetta, H. derbyanus, V. indica, F. fossa, P. larvata, V. zibetha, P. hermaphroditus*. Dosages used for these species range from 4 to 9 mg/kg (Kreeger, 1999). Smaller species often require higher doses, up to 12 mg/kg (McKenzie and Burroughs, 1999).

Isoflurane can be administered as an induction agent, via face mask, to small species or young animals. For small to medium-sized animals, chamber induction can also be readily performed if adequate equipment is available.

Supplemental anesthetic drug administration is typically performed using the same agents as those used for induction, albeit at lower doses (Palomares, 1993). When drug combinations have been used for initial injection (e.g., ketamine-medetomidine-butorphanol), either the entire combination is given at lower doses or

Table 37.2. Drug combinations reported for use in viverrids.

Drug Combination (Dose)	Species	Comment	Reference
Ketamine (10–15 mg/kg)	1) Viverrids		1) Denver, 2003
Xylazine (1–2 mg/kg)	2) P. jerdoni	2) Induction: 3–15 min. Recovery: 49–138 min.	2) Mudappa and Chellam, 2001
Ketamine (3–8 mg/kg)	A. binturong	binturong Lower ketamine and higher medetomidine doses provide shorter recovery	
Medetomidine (0.0206 mg/kg)		,	Klaphake et al., 2005
Butorphanol (0.2–0.5 mg/kg)			
Ketamine (10 mg/kg)	Viverrids		Denver, 2003
Diazepam (0.5 mg/kg)			
Ketamine (10 mg/kg)	Viverrids		Denver, 2003
Midazolam (0.25–0.50 mg/kg)			
Tiletamine/zolazepam			
1) 3–5 mg/kg	1) Viverrids		1) Denver, 2003
2) 5 mg/kg	2) V. tangalunga	2) Induction: 15-20 min. Need	2) Colon, 2002 and Colon, pers.
-,		redosing if excited, silence during induction. Recovery: 60–120 min. More docile in trap than <i>A. binturong</i> or <i>P. larvata</i>	comm.
3) 15 mg/kg	3) Madagascar carnivores		3) Louis, pers. comm.



Figure 37.1. Intubated meerkat (Suricata suricata) being maintained on inhalant anesthesia. A pulse oximeter and stethoscope are being used to monitor anesthetic depth. (Courtesy of Maud Lafortune, Houston Zoo.)

the anesthetic agent (ketamine in this example) is given alone. If the animal can be manually restrained, gas anesthetics can be used as a supplement.

In captivity, animals can be intubated and maintained on inhalant anesthetics (e.g., isoflurane) for several hours if needed (Figure 37.1). In cases in which gas anesthesia is not available, animals can be supplemented with low doses of intramuscular (IM) or IV ketamine as this anesthetic agent is metabolized relatively quickly (30–45 minutes).

COMPLICATIONS

Reports on anesthetic combinations in viverrids are sparse and no contraindications have been reported for any type of anesthetic agent (Denver, 2003). However, binturongs and civets appear to need relatively high drug dosages (Seal and Erickson, 1969; Moresco and Larsen, 2003). High variability between individual animals has been reported for brown palm civets and binturongs (Mudappa and Chellam, 2001; Moresco and Larsen, 2003); individual binturongs also have considerable variability in drug responses between different anesthetic events. In the field, binturongs and masked palm civets seem more excitable than Malay civets (Colon, personal communication) The genet and the lesser Indian palm civet have been reported to have convulsions, excitement, and hyperthermia when anesthetized with phencyclidine alone; these convulsions were controlled with promazine (Seal and Erickson, 1969).

RECOVERY

Anesthetic protocols that include reversible agents are often preferable in order to shorten recovery times; however, many field experts often use tiletamine/

zolazepam (Louis, personal communication) owing to this combination's reliability and large margin of safety. In general, recoveries from tiletamine/zolazepam tend to be smooth, although they are often relatively long. There is no antagonist for tiletamine and although an antagonist is available for zolazepam (flumazenil), it is usually not used. Recovery should take place in a quiet enclosure and animals should not be released before full recovery has been achieved. Ketamine-medetomidinebutorphanol combinations that were reversed with atipamezole resulted in smooth recoveries in binturongs (Moresco and Larsen, 2003). If a dissociative anesthetic is administered in combination with a sedative, it is recommended that administration of sedative antagonists (atipamezole/naloxone) should occur after most of the dissociative agent has been metabolized (typically 30–45 minutes post-injection for ketamine).

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38

Hyenas

Nina Hahn, John M. Parker, Gregory Timmel, Mary Weldele, and Gary West

INTRODUCTION

A breeding colony of spotted hyenas (*Crocuta crocuta*) was established at the University of California, Berkeley (UCB) in 1985 with wild cubs collected in Kenya. The spotted hyena was selected for research because of unique morphological and behavioral characteristics. Female spotted hyenas are larger than and dominant over males. They lack an external vagina, and instead have a hypertrophied, penis-like clitoris through which they urinate, copulate, and give birth. This makes them a useful research model in which to study the general mechanisms of sexual differentiation, and the differential development of morphology and behavior.

Colony management has included annual physical examinations, which are always performed on anesthetized animals. Hyenas are also anesthetized for longer-term procedures, including dentistry, diagnostic imaging, and surgery. They are also routinely immobilized to collect blood and measurements essential to research. Nearly 2,000 anesthetic procedures have been performed in the more than 20 years that the UCB colony has been existent, and no mortality has resulted from anesthesia. Unique characteristics of spotted hyena (Crocuta crocuta) anesthesia are outlined in the following chapter. Anesthetic protocols for the brown (Hyaena brunnea) and striped hyena (Hyaena hyaena) are similar to the spotted hyena (McKenzie, 1993). The minor differences in the anesthetic management of aardwolves (*Proteles cristatus*) are also covered in this chapter.

TAXONOMY AND BIOLOGY RELATED TO ANESTHESIA AND HANDLING

Hyenas resemble large canids, but because they belong to the suborder Feloidae (with cats and mongooses) they are more closely related to domestic cats (*Felis [sylvestris] catus*) than dogs (*Canis familiaris*). Reports of hyena anatomy and physiology indicate similarities to cats as well as dogs in terms of retinal anatomy

(Calderone et al., 2003) and susceptibility to pathogens (Ferroglio et al., 2003; Hahn et al., 2003; East et al., 2004; Harrison et al., 2004; Troyer et al., 2005). However, hyenas are more cat-like in several ways, including dentition as well as physiological responses to xylazine and ketamine (see the following).

Therefore, it is appropriate that veterinarians use physical anesthetic techniques suitable for large dogs, yet rely on domestic cat references for drug choices and dosages.

VASCULAR ACCESS AND SAMPLE COLLECTION SITES

Fore- and hind-limb veins are both readily accessible for catheterization (Figures 38.1 and 38.2). The venous anatomy as it pertains to catheterization of the forelimb is comparable with that of the domestic cat (Figure 38.1). Catheterization of the cephalic vein can be performed with the relative ease of that of a large dog. However, care should always be taken when positioning the catheter to avoid the extensive branching and anastomoses of the superficial forelimb vessels (Figure 38.1).

The jugular, cephalic, and saphenous veins are accessible for blood collection and cannulation. Sublingual vessels are prominent and can provide quick vascular access for electrolyte and blood gas analysis during anesthetic procedures. Arterial pulses can be palpated midline on dorsal metacarpi; however, arterial cannulation has not been attempted by these authors. Cerebrospinal fluid can best be collected by cisternal puncture. The occipital protuberance, spinous process of axis, and wings of the atlas can be palpated in an intubated hyena despite the thick neck muscles.

RESTRAINT

Chemical restraint (anesthesia) is always necessary prior to performing any procedures on adult hyenas. Cubs less than 1 month of age can be manually restrained for



Figure 38.1. Three photographs of the spotted hyena forelimb. **A.** A hyena in left lateral recumbency. Note the right antebrachium for panel **(B)** orientation. **B.** An in situ cranial-medial view from the level of mid-elbow to proximal carpus. Note the prominent superficial veins (visualization aided by manual occlusion). **C.** The venous anatomy in situ. Only the skin and superficial fascia have been removed. In both panels **(B)** and **(C)**, extensive anastomoses and bifurcations can be observed.



Figure 38.2. Catheter placement in the saphenous vein of a hyena.

examination and minor procedures such as blood collection and vaccinations. Hyena cubs 2 to 6 months of age may be placed in a "squeeze-back" cage for hand injection with anesthetics as described in the following. Captive aardwolves can be restrained with nets and then

hand injected with immobilizing agents. Aardwolves often vocalize loudly when being approached by handlers, but are easily restrained with a capture net.

FIELD TECHNIQUES

The anesthetic procedures described for anesthesia in captive spotted hyenas (see Captive Hyena Immobilization and Anesthesia) are also used in the field (Berger et al., 1992; Place et al., 2002). A report of field immobilizations of spotted hyenas used much higher doses of ketamine and xylazine than reported in this chapter (Stander, 1991). The most commonly used agent for immobilization in the field, however, is a combination of tiletamine hydrochloride and zolazepam hydrochloride (Telazol, A.H. Robbins, Richmond, VA), given at an estimated dose 6.5 mg/kg (Kay Holekamp, personal communication; Van Horn et al., 2004). For field-use in spotted hyenas, Telazol (500-mg vial) is reconstituted with 2.5 ml of diluent instead of the labelrecommended 5 ml. The resulting solution provides 86.2 mg/ml of each tiletamine and zolazepam (combined 172.4 mg/ml Telazol). Adult spotted hyenas receive 1.8 to 2.0 ml, subadults 1.4 to 1.6 ml, and cubs approximately 1 ml of this solution. The actual dose

used is probably less than 6.5 mg/kg, and 5 mg/kg Telazol is recommended for captive spotted hyenas. Spotted hyenas can be darted with either a blowpipe or a CO₂-powered rifle. The blow pipe is only useful at distances of 1 to 5 m and only practical for animals that are very comfortable around the vehicle. It is always preferable to use the blowpipe because it is silent and allows the dart to hit the animal with a smaller, less traumatic impact. Spotted hyenas are darted in the early morning hours. They are allowed to recover in the shade, and are attended until able to walk. The Telazol dose for field use has also been reported as low as 2.5 mg/kg (Holekamp and Sisk, 2003; Harrison et al., 2004). Spotted hyenas are crepuscular or nocturnal in the wild. Hyenas that are not persecuted by humans can be baited to a specific area and darted for immobilization (McKenzie, 1993). Spotted hyenas should be darted from an enclosed vehicle. The immobilization team should be aware of the location of other hyenas so that they do not injure an immobilized animal (McKenzie, 1993). Drugs that have been used in baited hyenas include tiletamine and zolazepam in combination, etorphine and xylazine, or ketamine and xylazine (McKenzie, 1993).

Wild aardwolves are also darted for immobilization. Aardwolves are nocturnal and are darted while feeding at termite mounds (Anderson, 1992; McKenzie, 1993). Aardwolves are located with spotlights and are approached to within a distance of 15 meters (Anderson, 1992; McKenzie, 1993). When darting aardwolves, lightweight projectile darts are used and gun pressures should be adjusted carefully. Aardwolves are much smaller than spotted hyenas and can be injured with projectile darts. Darting aardwolves with the wind direction from behind the operator helps dart placement to be more precise (Anderson, 1992; McKenzie, 1993). An effective immobilization combination for free-ranging aardwolves includes ketamine, acepromazine, and diazepam (McKenzie, 1993).

BODY WEIGHTS AND BLOOD VALUES

Adult colony-born female spotted hyenas weigh 58 kg on average (range, 47.2–73 kg). Adult males weigh slightly less than females, averaging 47.6 kg (range, 42.3–56.3 kg). Aardwolves typically weigh between 7 and 11 kg. Striped hyenas are typically 35 to 45 kg in body weight and brown hyenas are 40 to 45 kg (Table 38.1). Serum chemistry, blood gas analysis, and

Table 38.1. Body weights of adult Hyenidae species.

	Adult Body Weight
Spotted hyena (female)	50-90 kg
Spotted hyena (male)	45-55 kg
Striped hyena	35-45 kg
Brown hyena	40–45 kg
Aardwolf	7–11 kg

complete blood count of the spotted hyena are similar to both cats and dogs (Tables 38.2 and 38.3). Clot formation is frequently encountered in specimens treated with EDTA; therefore, heparin is the preferred anticoagulant.

Table 38.2. Serum chemistry ranges for captive adult spotted hyenas under KXA anesthesia.

Serum Chemistry	Range	Units
Alk phos	14-136	U/L
ALT	65-162	U/L
AST	76-142	U/L
CK	149-419	U/L
GGT	1–7	U/L
Albumin	2.2-2.8	g/dl
Total protein	6.1-7.7	g/dl
Globulin	3.6-5.2	g/dl
Total bilirubin	0-0.2	mg/dl
Direct bilirubin	0-0.1	mg/dl
BUN	14-30	mg/dl
Creatinine	1.1-1.8	mg/dl
Cholesterol	165-300	mg/dl
Glucose	80-153	mg/dl
Calcium	9-10.9	mg/dl
Phosphorus	3.2-6.5	mg/dl
Chloride	106-118	mEq/L
Potassium	4.2-4.9	mEq/L
Sodium	140-149	mEq/L
A/G ratio	0.4-0.7	
B/C ratio	8.6-23.3	
Indirect Bilirubin	0-0.1	mg/dl
NA/K ratio	29-35	
Anion gap	14-24	mEq/l
TCO ₂	13-25	mEq/l

All parameters represent a 95% confidence interval of 210 samples collected from 103 animals over a 7-year period. All samples were treated with either heparin or EDTA. All analysis provided by IDEXX.

Table 38.3. Complete blood count ranges for captive adult spotted hyenas under KXA anesthesia.

Blood Value	Range	Units	
WBC	7,200-23,200	Thous./µl	
RBC	4.74-8.73	Million/µl	
HCT	23-46.5	%	
MCV	43-65	fl	
MCH	14.4-22.5	pg	
MCHC	32.3-35.4	g/dl	
Neutrophils	42-85	%	
Lymphocytes	5-48	%	
Monocytes	0–7	%	
Eosinophils	1–14	%	
Basophils	0–3	%	
Abs. neutrophils	3,942-16,353	/µl	
Abs. lymphocytes	512-7,708	/µl	
Abs. monocytes	0-1,068	/µl	
Abs. eosinophils	98-2,440	/µl	
Abs. basophils	0-504	/µl	

All parameters represent a 95% confidence interval of 210 samples collected from <100 animals over 7-year period. All samples were treated with either heparin or EDTA. All analysis provided by IDEXX.

CAPTIVE HYENA IMMOBILIZATION AND ANESTHESIA

The anesthetic regime established 20 years ago at UCB remains the protocol of choice for captive spotted hyenas. It consists of 4 to 6 mg/kg ketamine, 1 mg/kg xylazine, and 0.045 mg/kg atropine (KXA). The ketamine dose has been incorrectly reported as 10 mg/kg (Berger et al., 1992; Hahn et al., 2003). Hyenas 9 months of age and older are anesthetized using a reusable, aircharged dart/blow gun system prior to handling. Telinject (Telinject USA, Agua Dulce, CA) and Daninject (Daninject, Kolmarden, Sweden) systems have both been used successfully at UCB.

Prior to darting, it is usually best to isolate the hyena in a small enclosure. Hyenas are fasted overnight prior to anesthesia. Xylazine appears to be an emetic in hyenas, as in cats (Plumb, 2005), and they frequently vomit after successful darting.

The hind quarters are the preferred anatomical site for dart placement. The excitement preceding darting often induces pronounced side-to-side whipping of the hyena's neck. This precludes the neck or shoulder region from being the preferred target site. Hyenas appear to undergo segmental anesthesia following KXA inoculation delivered into hind quarters; loss of function is first evident in the caudal region (lumbosacral region, pelvic limbs, and tail).

Mature hyenas are anesthetized with KXA using 3-ml darts and drug preparations of 100 mg/ml ketamine, 100 mg/ml xylazine, and 15 mg/ml atropine. Dart preparation time can be safely performed by first adding calculated doses of xylazine and atropine based on previous weights to the dart syringe, then adding ketamine to fill the remaining 3 ml volume (2.2–2.4 ml). Therefore, heavier hyenas receive a lower dose and often need supplemental doses of ketamine (1-2 mg/kg) for full sedation. In contrast, low weight animals often require supplemental sedatives, to counter the side effects associated with ketamine, such as rigidity and twitching. Intravenous diazepam (0.1-0.5 mg/kg) is commonly used for this purpose. When supplementing KXA anesthesia, diazepam causes a transient respiratory depression evident by prolonged periods of apnea. Subadult animals may not require the amount of ketamine needed to fill the dart to capacity. Less concentrated preparations of xylazine (20 mg/ml) and atropine (0.54 mg/ml) should be used for small cubs. Hyena cubs can be either hand or squeeze-cage restrained and drugs can be delivered via hand injection. Additionally, cubs generally require approximately 80% of the weight-calculated adult ketamine and xylazine doses. However, the previously stated adult dose of atropine is used for cubs.

Hyenas are muzzled on immobilization and when applicable, remain muzzled for the duration of the procedure when maintained on injected anesthetics. The bite response is not as readily abolished by ketamine anesthesia, as it is with dogs, cats, and primates. Jaw tone should be cautiously and properly assessed prior to endotracheal intubation. Hyenas are deeply anesthetized with isoflurane (2%–3%) delivered by mask prior to intubation.

Yohimbine (0.11 mg/kg), up to a maximum dose of 6 mg, is administered intramuscularly to reverse the xylazine at the conclusion of the procedure, at least 20 minutes after the last injection of ketamine. The time delay and route of administration decrease the likelihood of negative reaction owing to the presence of ketamine. Atipamezole or tolazoline can also be used to antagonize α_2 -agonists (Stander, 1991) (Tables 38.4 and 38.5).

Telazol (5 mg/kg) has been used successfully to anesthetize "ketamine reactors" (see the following), but was associated with a rough, prolonged recovery in the captive colony; therefore, it is not recommended.

Captive aardwolves are immobilized with Telazol and medetomidine in combination or ketamine and midazolam together (Table 38.3).

ANESTHETIC MAINTENANCE

For long-term and major surgeries, hyenas are catheterized, intubated, and maintained on isoflurane anesthesia (1%–2%) after darting with KXA as described. Yohimbine given after isoflurane stabilization may help prevent xylazine-induced adverse effects such as bradycardia, respiratory depression, and loss of thermoregulation, as described in the following.

Table 38.4. Anesthetic agents used in Hyenidae.

	Telazol	Ketamine and Xylazine	Ketamine and Diazepam and Acepromazine	Etorphine and Xylazine	Ketamine and Midazolam	Telazol and Medetomidine
Spotted hyena	2–5 mg/kg	4–6 mg/kg and 1 mg/kg		3 mg and 30 mg total dose	5 mg/kg and 0.2 mg/kg	1–2 mg/kg and 0.01 mg/kg
Striped hyena	2-5 mg/kg					
Brown hyena	2–5 mg/kg					
Aardwolf	2-5 mg/kg		15 mg/kg and		5 mg/kg and	1 mg/kg and
			0.15 mg/kg and		$0.2\mathrm{mg/kg}$	0.01 mg/kg
			0.15 mg/kg			

Table 38.5. Antagonists Used for Hyenidae Species.

Atipamezole	0.1-0.2 mg/kg IM
Yohimbine	0.11 mg/kg IM
Tolazoline	0.5-1.0 mg/kg IM
Naltrexone	100 mg per 1 mg etorphine

Intubation of the spotted hyena can be performed using a size 11 to 12 mm endotracheal tube with the relative ease of a large dog. Aardwolves accommodate a size 4- to 7-mm endotracheal tube. Hyenas are best intubated while in sternal recumbency. The larynx is easily visualized through the mouth using a large-bladed laryngoscope. Unlike cats, laryngeal spasm during intubation has not been observed.

ANALGESIA

Analgesia is always provided following major surgeries and dental procedures. Buprenorphine (0.01 mg/kg subcutaneously [SQ] or intramuscularly [IM]) is administered at the time of intubation and repeated following the end of surgery. If additional analgesia is indicated, 10 mg/kg etodolac (Etogesic) is administered orally once daily in food. No ill effects have been observed in any hyena receiving etodolac, including one hyena given 9 mg/kg daily for 1 month. Meloxicam (0.2 mg/kg SQ) has been used for endodontic procedures. It is given once at the completion of the procedure.

COMPLICATIONS

Xylazine frequently induces emesis, pronounced bradycardia, and loss of thermoregulation in hyenas. Atropine is included to reduce salivation typical of ketamine and offset bradycardia associated with xylazine administration. Arrhythmias and increased blood pressure have been associated with the combination of anticholinergics with α_2 -agonists in cats and dogs. However, these detrimental effects have not been observed in spotted hyenas immobilized with the combination of atropine with xylazine and ketamine. Aspiration of regurgitate was noted on necropsy in one geriatric animal (21 years old) with biliary carcinoma following immobilization with KXA, but aspiration following KXA administration has never been a clinical problem in hyenas. However, as a precaution hyenas are always fasted prior to immobilization.

Hyenas' eyes remain open after ketamine administration, as do cat eyes (Plumb, 2005), and should always be treated with ophthalmic lubricant (e.g., Lacri-lube). Prolonged apnea is noted infrequently following bolus diazepam and ketamine/diazepam administration as occurs in cats.

Hyperthermia in response to KXA administration has been observed. Care is taken to avoid darting during hot weather, but hyperthermia has been noted on days

when ambient temperature is not a contributing factor. Hyperthermia has been attributed to agitation and increased activity prior to darting; however, this may be a response to ketamine, as has been observed in cats (Plumb, 2005). Xylazine causes loss of thermoregulation in many animal species (Plumb, 2005), and this may also contribute to hyperthermia in anesthetized hyenas.

Very rarely, respiratory depression after KXA administration is noted. Reversal of the xylazine with yohimbine will correct this. Heart rates as low as 48 beats per minute are often observed, but as clinical outcome for these animals is no different from animals with higher heart rates, this has been attributed to the effects of xylazine and considered normal. Systolic heart murmurs have been identified occasionally during physical examination under KXA anesthesia. Follow-up cardiac ultrasound examinations identified a decrease in ventricular myocardial contractility in the three animals examined. This was attributed to the xylazine component of the anesthetic combination and not considered clinically significant.

Two types of adverse reaction to KXA anesthesia have been observed. Some hyenas display tonic-clonic-like movements, and extensor rigidity after KXA administration. This response is not uncommon in male hyenas. Male hyenas weigh on average less than female hyenas; therefore, they may receive the high end of the 4 to 6 mg/kg ketamine range when following the UCB KXA protocol. The adverse ketamine reaction observed in these hyenas may be caused by the ensuing relatively high ketamine-to-xylazine ratio. This reaction may be similar to what has been described in captive macaque monkeys (Macaca mulatta) who undergo frequent exposure to ketamine anesthesia. In macaques ketamine causes varying degrees of muscle rigidity in susceptible individuals. These animals may have a tonic-clonic or psychotomimetic response to the administration of ketamine (UC Davis Veterinary School, Clinical Medical Primatology lecture notes). Cats also demonstrate "myoclonic jerking and/or tonic/clonic convulsions" (Ketaset package insert) with ketamine administration.

Two male hyenas (brothers with the same parents but from different litters) developed generalized seizures after KXA administration. They both had been anesthetized with KXA numerous times. Both of these animals developed generalized seizures when anesthetized with KXA in their fourth year. Prior to having seizures, neither of these two animals demonstrated the tonic-clonic movements as described. Hyenas at the UCB colony are routinely immobilized for research purposes seven times the first year, four times the second year, twice the third year, and yearly thereafter. Seizures have been reported to occur in 20% of cats anesthetized with therapeutic doses of ketamine (Plumb, 2005). Ketamine is known to be epileptogenic (Plumb, 2005), and there may be individual susceptibility to the effects of ketamine in hyenas, but the

mechanism of both the seizure activity and tonic-clonic movements are purely speculative.

Diazepam (0.5–1 mg/kg IV to effect) eliminates seizures as well as tonic-clonic muscle activity in hyenas. Diazepam should always be kept close at hand when anesthetizing hyenas.

RECOVERY

Spotted hyenas are placed in a straw-bedded, enclosed cage for post-surgical recovery. Aardwolves are allowed to recover from anesthesia in a crate or medium-sized dog kennel. Animals are allowed to fully recover from anesthesia prior to being reintroduced to cage mates. After short-term procedures using xylazine, reversal can generally be within 1 to 2 hours of anesthesia. In longer-term or major surgical procedures when xylazine reversal is not used, or if opioid analgesics are used, hyenas are allowed overnight recovery prior to reintroduction to cage mates. After laparotomy hyenas are kept separate from cage mates for up to 2 weeks.

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Felids

Conny Gunkel and Maud Lafortune

ANATOMY AND PHYSIOLOGY RELATED TO ANESTHESIA

The group Felidae is comprised of 37 species. For clinical purposes, the group is divided into two subgroups, the small felids and large felids. The small felids include 29 species in the genus Felis and weigh less than 20 kg. They include the serval, *Felis Serval* (19 kg), ocelot *F. pardalis* (13 kg), domestic cat, *F. catus*, and many other small cats.

The large felids include eight species belonging to the genus *Felis*, *Neofelis*, *Panthera*, and *Acinonyx*. They include the mountain lion, *felis concolor* (103 kg), clouded leopard, *Neofelis nebulosa* (15–23 kg), snow leopard, *Panthera uncia* (25–75 kg), tiger, *Panthera tigris* (65–300 kg), leopard, *Panthera pardus* (37–90 kg), jaguar, *Panthera onca* (35–150 kg), African lion, *Panthera leo* (120–250 kg), and the cheetah, *Acinonyx jubatus* (35–72 kg).

The anatomy and principles of anesthesia in exotic felids are similar to that of domestic cats and are usually uneventful, with the exception of the tiger. This species appears to have more anesthetic complications than other felid species, including seizures and apneic episodes. Tiletamine-zolazepam has reportedly caused unexplainable sudden death in tigers and is therefore contraindicated to use in this species (Wack, 2003). There has also been some possible re-sedation in cheetahs and lions. The major differences while working on non-domestic felids compared with domestic species are the safety precautions needed when working with large cats. Different species have variable aggression levels. At some institutions, handlers enter cheetah enclosures and drive them into squeeze cages or crates (Meltzer, 1999).

PHYSICAL RESTRAINT

As a general rule, wild felids are darted in their environment from blinds or bait sites or they may be trapped and hand injected. Captive animals may be darted, pole syringed, or hand injected. Small felids, docile

individuals, and juveniles may be manually restrained for hand injection or gas induction.

Remote Darting

Remote darting is commonly used for felids over 20 kg (McKenzie, 1993; Nielson, 1999). A rifle, blow gun, or blowpipe can be used depending on the distance, but the dart velocity must be controlled to prevent excessive trauma and leg fractures (Meltzer, 1999). The most common injection sites are the muscle masses of the hind limb, and less commonly the shoulders in large felids. The dart size limits the volume of drug to be injected, and is generally 3 or 5 ml. Advantages of darting include safe drug administration for the operator, reduced stress, and ability to remotely immobilize an animal. Disadvantages include dart failure (multiple shots may be needed), and chances of soft-tissue trauma or fracture (Meltzer, 1999; Nielson, 1999).

Squeeze Cage, Kennel, and Traps

Squeeze cages allow for pole syringe or direct intramuscular (IM) injection. Advantages of this technique include less chance of injection failure or trauma as injection is direct, but disadvantages may include increased stress compared with darting, and risk of injury (broken teeth) from the metal bars during induction. Baited cage traps are the best catching method for many free-ranging small cats (DeWet, 1993; Ferreras et al., 1994; Beltran and Tewes, 1995; Nielson, 1999; Grassman et al., 2004). Captive cheetahs can be induced in a small cage, while being held down using wooden sticks (Meltzer, 1999). The tail and hind legs are pulled through the bar and the anesthetic can be injected intravenously (IV) into the medial saphenous vein.

Manual Restraint

Small cats less than 16 kg and juvenile large felids can be netted or hand grabbed by experienced handlers using gloves or towels (McKenzie and Burroughs, 1993; Fowler, 1995; Langan et al., 2000). Anesthesia can be

induced either by direct IM injection or gas inhalation. Advantages of manual restraint include speed and accuracy of injection, but staff must be experienced and careful to avoid trauma from sharp teeth and claws. The overall experience for the felid may be more traumatic and the cardiovascular side effects (arrhythmogenic effect, hypotension) of gas induction may be more severe than if it had been darted. Induction chambers are a valuable alternative for small patients who do not tolerate physical restraint or hand injection.

Behavioral Training for Injection

Captive felids can be trained for voluntary IM or IV injection. Tigers, cheetahs, African lions, cougars, leopards, and other species have been trained for this procedure (Figure 39.1). Clinically, stress is decreased, inductions are smoother, lower dosages are possible, and the veterinarian is not perceived as a threat, which is advantageous for later visual rechecks. Behavioral training for injection is the ideal method for induction and should be encouraged in all captive institutions. This requires dedicated time from animal trainers, consistency in routines, and animals that are willing to participate in these routines.

Oral Sedation

Although oral sedation has shown to be effective in domestic cats (especially detomidine 0.5 mg/kg and ketamine 10 mg/kg), in exotic felids oral sedation is mostly used as a pre-medicant to decrease the stress of darting to the animal rather than as a sole induction agent (Wetzel and Ramsay, 1998; Grove and Ramsay, 2000). Its unreliable administration and absorption makes it less predictable to use as a sole induction agent in potentially dangerous felids.



Figure 39.1. Training session for voluntary intramuscular injection. The leopard is trained to lie down and touch the target pole with its snout. The trainer then takes a pole syringe with a blunt needle and verbally cues the animal that it will get touched. A whistle is used as a bridging tool for positive reinforcement. The procedure is repeated two to three times, and food is used as a reward during the training session.

ANESTHETIC AGENTS

Many combinations of drugs have been used for immobilization of exotic felids. The choice of drugs is often dictated by availability, experience with a certain combination, cost of drugs, size and species of felids, length and purpose of procedure, and finally health status of the animal. When determining a drug dosage, the wild felid may require a higher dose of drugs than its captive counterpart. In general, small wild felids require a higher dosage of anesthetics per kilogram of body weight than large felids. Most protocols include a dissociative (ketamine or tiletamine) and an α_2 -agonist, benzodiazepine, opioid, or a combination of these. This part of the chapter describes commonly used protocols. The reader is referred to the chapter on pharmacology for general information on the anesthetic drugs.

Injectable Agents

Ketamine Ketamine used as sole anesthetic agent is reported in domestic and exotic felids, but its use requires high dosages (11–44 mg/kg) (Thurmon et al., 1996), which has major disadvantages. It provides a rigid and cataleptic state of anesthesia and has several side effects, including excessive salivation, seizures, muscle rigidity, and rough recoveries (Wildt et al., 1988; Epstein et al., 2002). Therefore, it is recommended to combine ketamine with an α_2 -agonist, benzodiazepine, and/or opioid to provide synergistic effects and a smoother anesthesia, while reducing the overall dose of ketamine. Ketamine is mainly excreted unchanged by the kidney in cats and should be used with caution in animals in renal failure.

Supplementation and Maintenance Ketamine is very useful for supplementation or maintenance of anesthesia at a dosage of 0.2 to 2.0 mg/kg IM or IV (Thurmon et al., 1996; Quigley et al., 2001; Miller et al., 2003).

Ketamine-Medetomidine Combinations Ketaminemedetomidine combinations provide reliable sedation for most species of exotic cats, particularly the large felids (cheetahs, cougars, lions, and tigers). Anesthesia with this combination is characterized by a smooth induction (5–15 minutes) and good muscle relaxation. The anesthesia lasts at least 45 minutes, after which supplemental agents may be necessary. Advantages of this combination include smooth induction and recovery, good anesthetic depth, analgesia, low dart volume (using concentrated ketamine at 200 mg/ml in the United States and medetomidine at 20 mg/ml in the United States or 10 mg/ml in Europe), reversibility with atipamezole, and the use of a low ketamine dose (Zoopharm, Fort Collins, CO). Disadvantages include the side effects of α_2 -agonists, which include vomiting (more frequently during induction), cardiovascular changes (peripheral vasoconstriction, pale-bluish mucous membranes, difficulty visualizing veins, falsely low pulse oximetry readings) and often severe hypertension, bradycardia, bradyarrhythmias, decreased cardiac output, mild to moderate respiratory depression (decrease in respiratory rate and tidal volume), increased urinary output (to be corrected with adequate fluid administration), and sensitivity to noise (Klein and Klide, 1989; Jalanka and Roeken, 1990; Pypendop et al., 1996; Deem and Citino, 1998; Forsyth et al., 1999; Pypendop and Verstegen, 1999; Lamont et al., 2001; Sinclair, 2003; Curro et al., 2004). Medetomidine should be used with caution in patients with pre-existing cardiac conditions. Respiratory depression and transient apnea are usually more pronounced in the minutes following induction, and can be reduced by providing supplemental oxygen or by reversing the medetomidine. If the medetomidine is reversed early during the procedure, the animal must be maintained on supplemental drugs or it may arouse. In captive settings, medetomidine is often reversed as soon as the animal has been intubated and maintained on gas anesthesia while in field situations, reversals are generally not given until the end of the procedure. The authors recommend dosages of 3 mg/kg ketamine and 0.03 mg/kg medetomidine IM for large felids. Reported dosages for large felids range from 1.5 to 6.0 mg/kg ketamine and 0.02 to 0.06 mg/kg medetomidine IM, whereas dosages in small felids range from 2.5 to 4.5 mg/kg ketamine and 0.05 to 0.07 mg/kg medetomidine (Tomizawa et al., 1997; Forsyth et al., 1999; Kreeger, 1999; Nielsen, 1999; Miller et al., 2003; Wack, 2005).

Ketamine-Xylazine Combinations Ketamine-xylazine combinations were used extensively before medetomidine was available and provided a similar anesthesia with similar side effects. Doses ranged between 3 and 10 mg/kg of ketamine and 0.3 and 1.0 mg/kg of xylazine in large felids; 4 and 26 mg/kg of ketamine and 1 and 4 mg/kg xylazine IM in small felids (Logan et al., 1986; Seal et al., 1987; Ferreras et al., 1994; Beltran and Tewes, 1995; Kreeger, 1999; Nielsen, 1999; Kearns et al., 2000; Grassman et al., 2004; Wack, 2005). Some clinicians prefer to administer the α_2 -agonists with midazolam as a first injection, followed 10 minutes later by ketamine in a second injection, in order to decrease the likelihood of seizures (Curro, 2002).

Supplementation and Maintenance The α_2 -agonist should not be supplemented for prolonged procedures. Instead, ketamine is recommended if unexpected arousal of the animal occurs before the procedure is complete. Propofol is a useful agent to increase the time of immobilization and prevent sudden arousals, but must be administered IV (Galloway et al., 2002; Wack, 2005). If prolonged procedures are anticipated, intubation and inhalant anesthesia are recommended.

Midazolam, diazepam or butorphanol has been added to the α_2 -combination to decrease the amount of

ketamine and/or xylazine and provide analgesic and sedative effects (Galloway et al., 2002; Langan et al., 2000; Ketz-Riley et al., 2003; Curro et al., 2004).

Ketamine-Midazolam Combinations. Ketamine-midazolam combinations are commonly used in small felids or debilitated large cats. It provides a smooth anesthesia with good cardiorespiratory functions. The benzodiazepine provides muscle relaxation and anticonvulsive effects. The combination of ketamine with midazolam is a good choice for any animal with suspected cardiovascular, neurological, or severe systemic diseases because of its wide margin of safety and cardioprotective nature (Thurmon et al., 1996; Forest, 2000). Midazolam is the drug of choice for IM injections because of its water and lipid solubility (Klein and Klide, 1989). Diazepam is not reliably absorbed from IM injection and should be reserved for IV use (Klein and Klide, 1989). Midazolam is now available as a 50 mg/ml concentration, and this permits lower injection volumes (Zoopharm, 2006). The ketamine dosage ranges between 5 and 10 mg/kg. The midazolam (or diazepam) dosage ranges from 0.1 to 0.3 mg/kg IM. The authors prefer the higher dosages because of subjectively observed better sedative effect. Butorphanol at 0.1 to 0.4 mg/kg or oxymorphone at 0.03 to 0.05 mg/kg can be included in the protocol or given after the initial injection to provide additional sedation.

Ketamine-Midazolam-Butorphanol Combination Ketamine-midazolam-butorphanol combination has the advantage of using three induction agents at a lower dosage. The butorphanol provides additional sedation and pre-emptive analgesia (Thurmon et al., 1996). The low total drug volume allows the entire combination to fit into one dart if using the more concentrated form of the drugs. This combination is recommended by the authors for healthy small felids and debilitated, very young, or geriatric large felids. It may not provide a reliable immobilization in healthy large felids.

Dosages range from 3 to 5 mg/kg of ketamine and 0.1 to 0.3 mg/kg of midazolam and 0.1 to 0.4 mg/kg of butorphanol (Pypendop et al., 1996).

Tiletamine-Zolazepam Combination Tiletamine-Zolazepam combination is especially useful in field situations in which short induction time and a reliable plane of anesthesia are ideal. It has a high margin of safety and few cardiopulmonary side effects (Smeller et al., 1996). Sudden arousals are rare with this combination but recoveries are often prolonged and stormy. Other disadvantages are pain at the injection site, increased risk of convulsion at higher doses, only partial reversibility (Tracy et al., 1988; Wack, 2003). In tigers, this drug has been reported to cause neurological conditions (seizures, ataxia) and death (often 2–4 days after anesthetic event) at high doses and its use in that species

is contraindicated (Curro, 2002; Wack, 2003). Similar signs seen in African lions. In domestic cats, the plasma half-lives for tiletamine (2–4 hours vs. 1.2 hours in dogs) and zolazepam (4.5 hours vs. 1 hour in dogs) are long, and may be the reason for the prolonged recoveries observed in felids (Baukema and Glazko, 1975; Thurmon et al., 1996). Dosages range from 1.6 to 4.2 mg/kg in large felids to 11 mg/kg for small felids (Smeller, 1976; Nielsen, 1999; Kreeger, 1999; Walzer, 2002; Schumaker, 2003; Grassman, 2004).

Combinations of tiletamine-zolazepam-ketamine with or without xylazine or tiletamine-zolazepam and medetomidine have been reported and have the advantage of decreasing the amount of tiletamine-zolazepam, smoothing the recovery, and shortening the recovery time (Röken, 1997; Deem and Citino, 1998; Taylor et al., 1998; Lewandowsky et al., 2002). The volume of the drug also fits well in most darts (Lewandowski et al., 2002). Ketamine (7 mg/kg) and tiletamine/zolazepam (0.9 mg/kg) are currently recommended for immobilization of free-ranging Florida panthers (*Felis concolor coryi*) (Taylor et al., 1998).

Medetomidine-Butorphanol-Midazolam Combinations

Medetomidine-butorphanol-midazolam combinations have been used experimentally on a few species of carnivores, including cheetahs, African lions, red wolves (Canis rufus), domestic and wild dogs (Lycaon pictus) (Itamoto, 2000; Lafortune et al., 2005; Citino, personal communication, 2006; Larsen, personal communication, 2006). In cheetahs, it provided a smooth and fast induction with an adequate plane of immobilization for 40 minutes, after which sudden recoveries were observed. Doses in cheetahs are 0.035 mg/kg of medetomidine and 0.15 mg/kg of midazolam and 0.2 mg/kg of butorphanol. Because this combination is fully reversible, it has great potential for use in short field procedures and/or animals with kidney or liver diseases. If the anesthesia has to be prolonged beyond 30 minutes, supplemental drugs (ketamine, propofol) or inhalation gas (isoflurane) are strongly recommended. Severe hypertension and occasional bradyarrhythmias may occur because of the medetomidine and may be corrected by reversing with atipamezole early into the procedure. Although in free-ranging work it may be advantageous to reverse all the induction drugs, in captive settings the sedative and analgesic effects of midazolam and butorphanol may benefit the patient, and for these reasons, may not be reversed.

Althesin Althesin (Saffan) is a combination of the two steroids alphaxalone at 9 mg/ml and alphadolone acetate at 3 mg/ml. This drug contains Cremophor to increase its solubility and must be given IV. The drug has a wide margin of safety and little cumulative effect, but because of the Cremophor can cause fatal anaphylactoid or anaphylactic reactions (severe pressure changes, bron-

chospasm, swollen paws and ears), especially in dogs (Swan, 1993). Further side effects observed are muscle tremors and salivation. The product is not available in the United States but is used in other countries, such as South Africa, where it is used for cheetahs at a dose of 6 to 8 ml per animal, which corresponds to 1.4 to 2.5 mg/kg of alphaxalone IV + 0.45 to 0.85 mg/kg of alphadolone acetate IV (Swan, 1993; Meltzer, 1999). This combination seems adequate for minor procedures. Alphaxan-CD RTU is a new product coming out soon in Australia, the United Kingdom, and South Africa, which appears to have the advantages of Saffan without the disadvantages of Cremophor owing to a different dissolution diluent (hydroxy propyl β cyclodextrin) and may be a promising drug in the future (Ferre et al., 2005).

Propofol This drug must be injected IV as well and a catheter is highly recommended for safe administration. If syringe drivers or infusion pumps are available, a constant rate infusion (CRI) can be used. Depending on the initial drugs used, a bolus of 0.2 to 2.0 mg/kg IV with a CRI dose of 0.02 to 0.2 mg/kg per minute can be given (Epstein et al., 2002; Galloway et al., 2002). Alternatively, manual boluses can be given at 1 mg/kg every 5 to 10 minutes. Propofol should be administered slowly, as to reduce the potential of hypotension and respiratory depression. Propofol is an alternative to isoflurane as a maintenance agent or to ketamine supplementation for animals with liver or kidney disease (Epstein et al., 2002). Propofol has no analgesic properties.

Inhalation Agents

Isoflurane, Sevoflurane, and Halothane Inhalant anesthesia is recommended for any lengthy and invasive procedure. Isoflurane and sevoflurane are commonly used and have replaced halothane because of reduced arrhythmogenic effects and metabolism. A non-rebreathing circuit may be used in felids weighing less than 4 kg, as it minimizes the resistance in the breathing system. The fresh gas flow for these are high (Bain: 150-200 ml/kg; Ayre's T-piece: 400 ml/kg) and may contribute to heat loss. If possible rebreathing systems should be used in bigger animals as they cause less heat loss, decrease pollution, and are more economical than the non-rebreathing circuit, but the bulky systems are not easily brought into the field. Because the induction drugs create a deep level of sedation, maintenance on isoflurane can be quite low initially (0.5%-1% for isoflurane and 0.5%-2% for sevoflurane), but will need to be increased as induction drugs begin to wear off.

Antagonists

With the use of anesthetic antagonists, clinicians are able to choose anesthetics that will provide quicker recoveries. Although advantageous in free-ranging procedures, reversing all anesthetic agents may not always be needed if the original induction agents have already been metabolized. Also, it may not be recommended if post-operative analgesia is desired. Although it is better to reverse α_2 -agonists to the profound sedation and significant side effects they create, opioids and benzo-diazepines may be left un-reversed to provide a smoother recovery. Opioids also provides pain management.

α_2 -Antagonists: Atipamezole, Tolazoline, and Yohimbine

All α_2 -adrenergic agonists can be reversed with multiple reversal agents, depending on their α_1 to α_2 specificity (Virtanen, 1988). Medetomidine has a high α_2 selectivity and should be reversed with atipamezole at 3 to 5 mg atipamezole per 1 mg of medetomidine used IM (or 0.1–0.45 mg/kg IM) (Jalanka and Roeken, 1990; Deem and Citino, 1998; Langan et al., 2000; Galloway et al., 2002; Miller et al., 2003; Curro et al., 2004). A lower dose may be used after a prolonged procedure, owing to partial metabolism of the medetomidine.

Atipamezole has CNS stimulating effects and may increase intracranial pressure; therefore, it should be used with caution in neurological patients (Keegan et al., 1995). Although reported in the literature, it is not recommended to give atipamezole IV because it can create excitatory side effects (Jalanka and Roeken, 1990; Sinclair, 2003). Finally, atipamezole can create tachycardia and hypotension (Klein and Klide, 1989). Yohimbine should not be used for medetomidine antagonism as its reversal effect is not reliable, ataxia is common and resedation may occur (Jalanka and Roeken, 1990).

Xylazine can be reversed with yohimbine or tolazoline because of their mixed α_1/α_2 specificity. Yohimbine can be used at 0.04 to 0.3 mg/kg IM or slow IV (Seal et al., 1987; Quigley et al., 2001; Lewandowski et al., 2002; Curro et al., 2004). Tolazoline (0.5–2 mg/kg IM or IV) is rarely used at it possess the least specificity for α_2 receptor and side effects, including central nervous system excitement, salivation, and muscle tremor have been reported (Thurmon et al., 1996; Paddleford and Harvey, 1999). The use of atipamezole to reverse xylazine is not recommended because it can lead to hyperexcitement or "over-alertness" and transient re-sedation 2 to 4 hours post-reversal (Klein, 1989).

Opioid Reversal: Naloxone, Naltrexone, and Nalmefene

Naloxone (0.002–0.04 mg/kg IM/IV is a pure antagonist that acts primarily on the mu receptor. Naltrexone (0.05–0.25 mg/kg IM/IV) is a μ -, δ -, and κ -opioid receptor antagonist and provides some advantages in comparison to naloxone, in that it is longer acting and is also active when given orally. Nalmefene (0.03 mg/kg IV) is another pure opioid antagonist with greater preference for μ - than δ - and κ -receptors and more potent and longer lasting than naloxone (Dyson et al., 1990; Thurmon et al., 1996). It is important to realize that antagonizing opioids not only reverse the effects of the

drug given, but also antagonize the endogenous opioid system, and this may cause hyperalgesia, hypersensitivity, and behavioral changes (Robertson, personal communication, 2006). To provide postoperative pain management and slight sedation the opioids in felids are rarely reversed at the end of the anesthetic event.

Benzodiazepines Reversal: Flumazenil and Sarmazenil

Flumazenil (0.01–0.2 mg/kg or 0.008 mg/1 mg of diazepam/midazolam IM) is a reversal agent for the benzodiazepines, but its high cost can be prohibitive to use (Tranquilli et al., 1992; Walzer and Huber, 2002; Lafortune et al., 2005). Flumazenil has not shown to improve recoveries in domestic cats and seem to have a very short half-life in cats (Ilkiw, 2002), which makes its use not very efficacious.

Sarmazenil has also been used effectively at 0.1 mg/kg IM to reverse zolazepam in cheetahs but is not currently available in the United States (Walzer and Huber, 2002). Fortunately, the benzodiazepines are rarely reversed at the end of the anesthetic event, much like opioids, because of their short duration of action and little sedative effects. The remaining benzodiazepine might be beneficial to smooth the recovery (Ilkiw, 2002), although one study showed a significantly shortened and better recovery when reversals were used (Walzer and Huber, 2002).

TECHNIQUES AND MONITORING

Pre-anesthetic Considerations

A pre-anesthetic evaluation of the animal is often limited, but some parameters can still be considered and may influence the anesthetic approach. Species, accessibility (free ranging vs. captive), health status, attitude, weight, fasting status, type of procedure, environmental factors, staff, and equipment availability can modify the choice of drugs, dosage, and route of administration.

Weight In captive situations, weight is often known from previous immobilizations or from having a scale within the enclosure, but in free-ranging wildlife, body weights are estimated. References are available to find average weights of felid species (McKenzie and Burroughs, 1993; Kreeger, 1999; Nielsen, 1999; Wack, 2003).

Fasting In a captive environment, food should be removed 12 to 24 hours before the procedure. Water should not be withheld but precaution should be taken to prevent the animal from accidentally drowning in the water bowl during induction. In free-ranging situations, fasting is often impossible. Vomiting/regurgitation are a common occurrence when using α_2 -agonist agents (medetomidine or xylazine) as the induction agent, and unfasted animals have a greater risk of aspiration or esophagitis (See Complication section).

Health Status If possible, a close observation of the animal should be obtained before any procedure is started, understanding that it may give limited information about the true physical status of the animal. Neurological signs, dehydration, blood loss, and/or diarrhea may be observed before the anesthetic event and may impact the drugs and treatment choices. Some felids can be trained for voluntary blood collections (Figure 39.2), and ideally pre-anesthetic blood parameters should be obtained.

Attitude Every effort should be made to keep the animal calm and relaxed. A very agitated and stressed animal usually needs more drugs and because of the high sympathetic tone during stressful periods, may have more cardiovascular and metabolic complications. If possible, a prolonged and stressful darting period should be aborted and the procedure rescheduled. If an animal is known to be easily agitated, an oral sedative such as acepromazine, midazolam or medetomidine can be used to decrease the risk of hyperthermia, hypotension or hypertension, arrhythmias, or seizure activity during the anesthetic episode.

Induction

Before approaching the anesthetized felid, it is prudent to touch the felid with a pole to check for a response to physical stimulus (ear twitch) (Nielson, 1999). When it is safe to approach, baseline data including heart rate, RR, temperature, color of mucous membranes, and capillary refill time should be collected immediately and then every 5 to 15 minutes (Nielson, 1999). After vital signs are taken and the animal is considered well sedated/immobilized for the procedure, eye ointment



Figure 39.2. Voluntary blood draw in a tiger. This tiger is trained to get into a small cage and lie down. The tail of the animal is pulled through the bars or a small opening in the cage and the veterinary technician is able to take a blood sample from the tail vein. The trainer is located at the front of the animal and rewards verbally and with food.

and blindfold are used to reduce stimulation and protect the eyes. Some workers also put cotton in the animal's ears to reduce auditory stimulus. It is not recommended to muzzle felids, as it may cause the tongue to fall back and obstruct the airways. Also, if the animal regurgitates, there is an increased risk of aspiration while muzzled (Nielson, 1999).

Supplemental Oxygen and Gas Anesthesia

It is recommended to supplement any injectable anesthesia with oxygen. This can be achieved using a nasal tube or face mask, or through an endotracheal tube. Supplemental or maintenance anesthesia can be used in a similar fashion with isoflurane or sevoflurane, although intubation is highly recommended.

Face Masks Domestic animal face masks can be used for small felids, whereas home-made ones are needed for large felids. A cut 1-gallon plastic jug with softened and taped edges works extremely well with lions and tigers. If a mask can not be placed on the animal's head because of safety considerations, the inhalant can be delivered through the circuit or long tubing into the cage (through the bars or the cage door) with the tip of the tubing in front of the nose of the animal. This way the level of sedation can be deepened until it is safe to place the mask on the head.

Nasal Supplementation Using an anesthesia machine or oxygen tank, the oxygen can be delivered through a small diameter plastic tube or small ET tube inserted in one of the nares. The flow rate should be 2 to 5 L/minute.

Intubation

Intubation of exotic felids follows the same guidelines as for domestic cats and can be relatively easily performed in lateral or sternal recumbency. Once an adequate depth of anesthesia is reached, intubation is performed with opening the mouth with two gauze strips, tape stripes, ropes, or towels. A mouth gag can be placed in the animal's mouth to prevent biting injury while intubating. Visualization of the glottis is performed preferably with a laryngoscope, while the tongue is pulled rostrally. A minimal amount of lidocaine can be sprayed or dropped on both arytenoids to avoid bronchospasm and/or laryngospasm. The tube is then inserted between the arytenoids and advanced into the trachea. Tube size varies with species and a range of different sizes should be readily available. Cougars need a smaller tube in comparison to their body weight (size 10-14 mm internal diameter), whereas tigers and lions require relatively large tubes (16–24 mm). Smaller felids are comparable to domestic cats and range from 4 to 10 mm. Once the tube is in place the cuff should be inflated to prevent leaks and aspiration of oral fluid. Over-inflation of the cuff should be avoided because of the risk of pressure necrosis and tracheal rupture. Secure tying of the tube behind the head or on the lower jaw is mandatory to prevent accidental extubation. The tube is then connected to the breathing circuit and oxygen started.

Transport

Felids are capable of early recovery during transport and safety precautions must be taken to deal with such a possibility. At a minimum, a secondary holding (crate, closed vehicle), net, catch pole, or stick should be used to slow down the animal and permit additional drugs to be given to the animal. Some institutions have firearms close by in case of arousal and direct danger to humans. Extra anesthetic drugs, and reversal and emergency drugs always should be readily available. Every institution or zoo should have a dangerous carnivore protocol and decide on their level of security while handling exotic felids.

Monitoring

Monitoring data include at a minimum: temperature (T), heart rate (HR), and respiratory rate (RR). Additional data such as pulse oximetry (SPO₂), end-tidal CO₂ (ETCO₂), electrocardiogram (EKG), blood pressure (BP), blood gases, and electrolytes are recommended for more reliable observation of cardiopulmonary values and their instrumentation can be portable (Figure 39.3).

Pulse Oximetry Although pulse oximetry has not been validated on exotic felids, its use is helpful to monitor



Figure 39.3. Monitoring equipment during cheetah anesthesia, including capnography, pulse oximetry, intravenous and intraarterial catheters, and electrocardiograph reading. Supplemental monitoring tools not shown in this picture include a pressure cuff and temperature probe.

trends and HR, but its limitations should be considered. Readings are not reliable in states of peripheral vasoconstriction (α_2 -agonists, hypothermia), anemia, and dry mucous membranes. Falsely low readings may occur and should be verified with a blood gas analysis (Langan and Citino, 2000; Lafortune et al., 2005). Oximetry probes can be placed on the tongue, ear, and vulva of females or prepuce of males. Rectal reflectance probes are also available.

Capnography Capnographs give a value for ETCO₂ and a CO₂ graph over time to assess the breathing pattern and ventilation. A capnograph or arterial blood gas is necessary to monitor ventilatory status (expired CO₂ or PaCO₂, respectively), as RR and SPO₂ are not valid predictors. Although it is best used with an endotracheal tube, the capnograph can be used with a nasal adaptor when the animal is not intubated. Acceptable values range from 30 to 50 mmHg, and supplemental breaths should be given if the ETCO₂ rises over 55 mmHg or PaCO₂ is over 60 mmHg.

Blood Pressure Blood pressure can be measured with a direct or an indirect method. The direct blood pressure measurement is the most accurate method and requires an arterial catheter placed into the dorsal pedal artery, the lingual artery, the femoral artery, or the coccygeal artery (Figure 39.4). This is recommended for any invasive and prolonged procedures, because it also permits blood sampling for blood gas analysis. The indirect blood pressure measurement is performed via Doppler or oscillometry. The Doppler is a very useful, small, and portable device that provides HR, cardiac rhythm, pulse strength, and regularity. Systolic blood pressure values can be measured with a hand-held manometer connected to a cuff placed above the Doppler crystal. In



Figure 39.4. Close-up view of the intra-arterial catheter placed in the dorsal pedal artery. The three-port valve permits direct blood pressure measurement and availability to sample arterial blood gases.

small feline species (less than 4 kg) the value obtained is considered to be closer to the mean arterial blood pressure than the systolic (Caulkett, 1998). Blood pressure cuffs (size 2–5 for small felids or human cuffs for larger felids) can be placed on the cranial limb or the base of the tail and should be considered a minimal monitoring requirement even in a field setting. Recent progress in technology has improved portability and readings under low HR or vasoconstriction. Until normal blood pressures in non-domestic felids are known, mean arterial blood pressure is ideally maintained between 60 and 150 mmHg to provide adequate organ perfusion and oxygen delivery to the tissues.

EKG can be obtained via the transportable multimonitor or a wireless (Biolog, Hayward, CA) device and reference values are available in cheetahs (Button et al., 1981; Schumacher et al., 2003). The EKG evaluates the electrical but not the mechanical activity of the heart. Abnormalities such as bradycardia, tachycardia, or arrhythmias can be detected and treated in an appropriate manner (see Complications).

Blood Gases and Electrolytes Blood gases and electrolytes evaluate the metabolic and respiratory status of the anesthetized patient. These values can change significantly over time and repeated samples (i.e., every 30 minutes) are highly recommended. A change of electrolytes (especially potassium) and base excess over time has been observed in certain species of exotic felids and may need further attention (see Complications). Portable on-site analyzers are inexpensive, accurate, and user friendly.

Body Temperature Body temperature of exotic felids is believed to be in the range of domestic felids. Hypothermia or hyperthermia can occur during anesthesia and the temperature should be monitored. Hypothermia can be reduced by using a circulating warm water blanket, warm water blankets, warm water bags, Bair Hugger, fleece blankets, and/or warm fluids. Hyperthermia can be managed by cooling the animal with cold water or alcohol, or using cold water enemas (Curro et al., 2004).

Vascular Access

Venipuncture sites are similar to that of domestic cats and include the jugular, cephalic, medial, and lateral saphenous veins, as well as the femoral veins (Fowler, 1995; Wack, 2003). Large exotic felids can also be bled from the lateral tail vein located at 2 and 10 o'clock (Fowler, 1995; Wack, 2003). Intravenous catheters (size 22–14 gauge) are placed into the cephalic, saphenous, tail vein, or less commonly into the jugular vein. Long-term catheters are best placed into the tail vein. Vessels of big cats can be surprisingly difficult to visualize despite their large size. The α_2 -agents cause peripheral vasoconstriction and can decrease visualization even

further. After reversal with atipamezole, the catheter is often easier to place. Fluid therapy during anesthesia follows domestic felid principles.

COMPLICATIONS

Common complications during general anesthesia in non-domestic felids are often related to the drugs used in the anesthetic combination, and include vomiting, cardiopulmonary changes, seizures, and blood gas and electrolyte variations.

Vomiting

Vomiting on induction is commonly seen in cats when α_2 -agonists are used (Thurmon et al., 1996; Tomizawa et al., 1997). The risk of aspiration is increased in nonfasted animals. To decrease the risk of post-operative morbidity, the esophagus should be flushed and cleaned, and residual gastric fluid content should be suctioned (intubation is necessary for this) to prevent esophagitis. The pharynx area should be examined to determine any potential aspiration and treated appropriately.

Cardiovascular Complications

Hypertension and Bradycardia Hypertension and bradycardia are common side effects of α_2 -agonists, and excessive values may need to be addressed. α_2 -agonist-related bradycardia (HR = 25-60 bpm) can be acceptable under these circumstances because it is drug induced, but a further decrease in rate or the development of bradyarrhythmias (e.g., second-degree heart blocks or premature ventricular contractions [PVC]) may have to be treated. The treatment with anticholinergics such as atropine is controversial (Sinclair, 2003). The authors believe that increasing the heart rate by using an anticholinergic in an animal with high vasoconstriction may highly increase the myocardial workload, increase arrhythmias, and severely increase the blood pressure, which further decreases the cardiac output. Therefore, we recommend against using anticholinergics to treat α₂-agonist-associated bradycardia but instead reverse the α_2 -agonists. It is important to remember that if the α_2 -agonist is reversed, the animal may arouse and supplemental drugs will be needed (inhalant anesthesia or propofol) to maintain adequate anesthesia. Aborting the procedure is also a possibility once the animal is secured.

Arrhythmias Changes in heart rate and rhythm unrelated to α_2 -agents can be treated depending on their nature. Bradycardia (less than 100 bpm in cats weighing less than 7 kg, less than 80 bpm in cats weighing 10 to 20 kg and less than 40–60 bpm in large felids) can be caused by a deep level of anesthesia, hypothermia, or cardiac-related issues, and should be treated accordingly. Lightening the depth of anesthesia and warming the

patient may normalize the heart rate. Simple bradycardia, sinus bradycardia, or first- or second-degree heart blocks should be treated with glycopyrrolate (0.005–0.01 mg/kg IV or IM) or atropine (0.01–0.04 mg/kg IV or IM) especially if the blood pressures are low. Glycopyrrolate does not reliably work in hypothermic animals and often causes a significant decrease in heart rate before the expected increase occurs. In conclusion, it is not necessary or advisable to give routine anticholinergics in felids and its use should be reserved for the treatment of non-medetomidine–related bradycardia only.

Complex arrhythmias such as atrial fibrillation or PVCs are not very common but can occur with changes in electrolytes, high levels of carbon dioxide, hypoxemia, or painful stimuli and should be watched closely. Underlying causes should be investigated and corrected, but treatment per se (lidocaine, glycopyrrolate) often is not necessary. A series of abnormal complexes with subsequent decrease in cardiac output (i.e., low BP, obvious deficit in pulse rate and pulse pressure) should be investigated and treated.

Tachycardia Tachycardia can be observed if the depth of anesthesia is inadequate and/or pain is present. Both should be corrected with appropriate anesthetic or analgesic drugs. Further causes include hypotension caused by hypovolemia, in which an IV fluid bolus or the administration of a colloid may normalize the increased HR.

Hypotension Hypotension is characterized by prolonged periods of low blood pressures (a mean BP less than 60 mmHg) and could be caused by excessive depth of anesthesia or hypovolemia. Fluid bolus can be calculated as 15 to 20 ml/kg over 15 minutes and further fluid administration should be given at 10 to 20 ml/kg per hour. An animal with pre-existing low protein may benefit from the administration of a colloid or plasma. If low HR accompanies the low blood pressure, a dose of glycopyrrolate may be efficient to increase BP via an increase of the sympathetic tone. Dopamine or dobutamine administered IV are also options to increase BP via the increase of cardiac output.

Cardiac Arrest Cardiac arrest is treated following the principles of cardiopulmonary resuscitation (see Chapter 7). Emergency drugs doses and volumes should be calculated before the start of the procedure (and ideally drawn up) and readily available.

Respiratory Complications

Hypoventilation Hypoventilation is common in large felids and is often caused by a deep level of anesthesia and can lead to increased CO_2 . If the RR is low and the $ETCO_2$ is above 55 mmHg, additional breaths should be given via a breathing bag, Ambu-bag, or ventilator.

Hyperventilation should be avoided to prevent the animal from becoming apneic.

Hyperventilation Hyperventilation and/or panting should be monitored closely and may result in a light plane of anesthesia, despite high vaporizer settings. Additional deep breaths in a "sigh-manner" should be given to increase the tidal volume, open the alveoli and improve gas exchange $(CO_2, O_2, \text{inhalants})$ in the lungs.

Respiratory Arrest Respiratory arrest is not uncommon in big cats and early recognition is easiest with close monitoring of respiratory rate and pattern. A capnograph may give an early warning of hypoventilation and alarm if apnea occurs. If not already, the animal should be intubated and ventilated. The depth of anesthesia should be assessed and corrected. If necessary, reversals may be given. Positioning into sternal recumbency may help. The acupuncture point (Jen Chung) on the nose can be stimulated with a needle and may initiate a breath (Davies et al., 1984). The use of doxapram is still controversial when used in a hypoxic state, and should be used as a last resort (Roll and Horsch, 2004).

Seizures

Seizures are commonly observed in many felids species, and especially in tigers (Jalanka et al., 1990; Ferreras et al., 1994; Quigley et al., 2001; Epstein et al., 2002). The seizures are believed to be triggered when high doses of ketamine or tiletamine-zolazepam are used (Epstein et al., 2002). Treatment of seizures includes diazepam or midazolam at 0.1 to 0.5 mg/kg IV for either drug. If an IV route is not available, midazolam can be given IM, orally, nasally or rectally. Supplemental oxygen should be administered if feasible. If the seizures cannot be controlled with the benzodiazepines, propofol can be given at 0.2 to 1 mg/kg IV. Thiopental sodium has been used in seizuring cheetahs at 1 to 2 ml IV of 5% injectable solution but is often not readily available in field or zoo situations (Meltzer, 1999). The addition of midazolam to the protocol may decrease the occurrence of seizures, and adding other sedatives to the combination may help decrease the ketamine dosage and thus the likelihood of seizures.

Electrolyte Imbalance

Potassium Elevation and Metabolic Acidosis Another complication in the authors' experiences is a change in blood gas and electrolytes over time. This syndrome has mainly been observed in tigers, cougars, and cheetahs, and close following of arterial blood gases and electrolytes are advised for these species (every 15 to 30 minutes), because clinical signs are seen. All animals evaluated had normal blood potassium initially. A steady but significant rise in potassium (greater than 6 mmol/L) has been observed in 20% of the animals

over time. No obvious clinical signs were observed during anesthesia, but EKG abnormalities (spiked T wave, bradyarrhythmias, and widened QRS complexes) were noted in some animals. Left untreated, hyperkalemia, especially in combination with severe acidosis, can lead to cardiac arrest. If potassium raises greater than 6 mmol/L or a change in EKG complexes is observed, treatment with insulin in dextrose (0.1–1 unit of regular insulin/kg in 500 ml of 5% dextrose fluids) or 0.25-1 g/kg dextrose diluted very slowly until potassium decreases is necessary to avoid cardiac arrhythmias and arrest. Calcium gluconate can be used in addition to protect the heart from arrhythmias via increasing the depolarization threshold, but will not address the hyperkalemic state. Metabolic acidosis has also been reported in tigers and cheetahs, but a correction of the bicarbonate should be kept conservative until reference values for the different felid species are known (Curro et al., 2004; Lafortune et al., 2005). Rather, it should be the goal to investigate if underlying causes such as preexisting renal, liver, or gastrointestinal diseases are present and treat these accordingly (Epstein, 2002).

SEDATION

Under certain circumstances it is necessary to sedate an animal to relieve anxiety, decrease motor activity, reduce post-operative wound licking, and reduce agitation.

Benzodiazepines such as midazolam or diazepam in oral formula have been used in treats or food for long duration at 0.15 to 0.5 mg/kg PO. The benzodiazepines have only mild sedating effects but are useful for the anxiolytic and appetite stimulating effect (Klein, 1989). Long-term oral administration at higher doses has been associated with detrimental acute fulminant hepatic failure in domestic cats (Center, 1996). Therefore, cats showing signs of sedation, lethargy, vomiting, and anorexia in the first week of treatment, should be discontinued from the treatment (Center, 1996).

Neuroleptic or antipsychotic drugs such as the phenothiazine derivatives have calming and mood-altering effects via their mechanism of action as a dopamine antagonist. Acetylpromazine can be used in a dosage of 0.03 to 0.1 mg/kg IM or 0.1 to 0.2 mg/kg PO and produce mild to moderate sedation for up to 6 to 8 hours in cheetahs (Meltzer, 1999). It is useful at lower doses for its ability to "take the edge off" or calm an aggressive animal without causing heavy sedation. Azaperone has been used at 3 mg/kg to smooth rough recoveries from tiletamine-zolazepam combo in African lions (McKenzie and Boroughs, 1993). Long-term sedation is not commonly used in felids owing to their adaptability and the unpredictable side effects of these drugs.

Cheetahs seem to be the exception and may require tranquilization to reduce their stress. Perphenazine enanthate has been used at 3 mg/kg IM for long lasting sedation for up to 14 days without side effects (Huber

et al., 2001). Zuclopenthixol acetate is not recommended for sedation in cheetahs owing to severe side effects, including inappetence, ataxia, extrapyramidal reactions, akathisia (motor restlessness), and prolapse of the third eyelid (Huber et al., 2001). Until further research is performed in other felidae, it would be prudent not to use this drug in any felid species.

PAIN MANAGEMENT

The importance of pain management is well recognized and an analgesic should be included in the anesthetic protocol if a painful procedure is being performed. Providing analgesia to exotic felids is essential because, in addition to managing pain, it also quickens recovery and healing, prevents self-mutilation and permits an earlier return to feeding (and ability to take medication PO). Many anesthetic agents such as isoflurane or propofol do not have acceptable analgesic properties and additional drugs are necessary. Unfortunately, acute and chronic pain in zoo animals and wildlife is often still under-treated. The lack of research studies involving exotic species, difficulties in recognition and assessment of pain, and the concern for potential side effects are some of the reasons why clinicians may shy away from prescribing pain management. Nevertheless, there are currently several options for treating pain in domestic cats. A better understanding of their unique metabolism and drug response may benefit non-domestic species (Robertson, 2005).

Some extrapolations from domestic cats are made in this chapter and are combined with the personal clinical observation of the authors in the hope of providing guidance for pain management in exotic cats.

Opioids

Opioids have historically and unjustifiably been blamed to cause "opioid mania" and excitatory effects in cats, whereas in fact this was owing to excessive doses administered (Fertziger et al., 1974). Recent research in domestic cats has shown that with appropriate doses, analgesia can be created with limited side effects and innocuous behavior changes such as purring, rolling, and kneading (Robertson, 2005). Side effects may include salivation, mydriasis, and hyperthermia. Commonly used opioids in domestic cats are buprenorphine, hydromorphone, oxymorphone, morphine, methadone, meperidine, fentanyl, and butorphanol. In order to maintain appropriate analgesia opioids should not be reversed postoperatively in animals undergoing invasive painful procedures. Buprenorphine is a partial µ-receptor agonist and used widely in domestic cats. In these animals, its analgesic properties have been shown to be superior to other opioids (Robertson, 2005). Buprenorphine has few side effects, a long duration of action, and oral or buccal absorption (Robertson and

Lascelle, 2005). Its absorption in cats is slow when given intramuscularly (45 minutes), but faster when given intravenously or bucally (10 minutes), and lasts about 6 hours (Robertson, 2005). Although no studies on buprenorphine in exotic felids could be found, the authors have used it routinely at 0.01 to 0.02 mg/kg IV/IM/PO in clinical cases for intra-operative and postoperative pain management in captive non-domestic cats. Oxymorphone and hydromorphone are used at 0.05 to 0.1 mg/kg IV or IM in domestic cats and provide good analgesia and some sedation for severe pain such as fractures, soft-tissue trauma, and other major surgeries. Drugs can be given IV to produce greater intensity and duration of antinociceptive effects (Robertson, 2005). Oxymorphone use in cats appears to be associated with fewer side effects and may be superior to hydromorphone (Posner, clinical observation, 2005; Robertson 2005).

Fentanyl can be given as a CRI intra-operatively to provide additional potent but short-acting analgesia. It is given at a bolus of 2 to 5 μ g/kg, followed by a constant rate infusion (CRI) at 0.1 to 0.3 μ g/kg per minute during surgery (Galloway et al., 2002).

Butorphanol, a κ-receptor agonist and μ-antagonist, is also commonly used and is beneficial in treating mildly painful conditions and appears to be quite effective for visceral pain, while creating almost no behavioral side effects. Its slight sedative effects and concentrated form makes this drug a good adjunct for induction drug combinations (0.1–0.4 mg/kg IM or IV). Because of its short duration of action (less than 90 minutes) and limited analgesic properties, it should only be used for mild pain (Lascelles and Robertson, 2004; Robertson, 2005) or in addition to other drugs such as NSAIDs and local blocks. This drug exhibits a ceiling effect, which means that increasing the dose above 0.4 mg/kg will not produce any further analgesia. Butorphanol usually does not need to be reversed at the end of a procedure because of its short duration of action and minimal behavioral effects.

Tramadol and fentanyl patches have been used anecdotally in exotic felids and may be other options for pain management, but their use must be done with caution because no research has been done on non-domestic felids.

Non-steroidal Anti-inflammatory Drugs

Non-steroidal anti-inflammatory drugs (NSAIDs) are the preferred class of analgesics in non-domestic species because they provide long-lasting anti-inflammatory and analgesic effects (up to 24 hours) (Robertson, 2005) and do not fall under controlled substance regulations. Because of the cats' inability for glucuronidation, metabolism of several NSAIDs occurs more slowly in cats compared with other mammals and should be considered when choosing a dosage and dose intervals (Court

and Greenblatt, 1997). Because of the well-known side effects of NSAIDs such as gastrointestinal ulcerations, nephropathies (renal medullary necrosis), and impaired coagulation, they are usually recommended for short-term use with close monitoring of the patient.

Most commonly used NSAIDs in cats are meloxicam, carprofen, and ketoprofen, and doses are extrapolated from the domestic cat studies, since no study could be found in exotic felids. Meloxicam is given at 0.2 to 0.3 mg/kg SC/IV pre-operatively and can be continued once a day at 0.1 mg/kg SC or PO for a maximum of 3 days (Burgos-Rodriguez et al., 2004; Robertson, 2005).

Although the long-term use of meloxicam has not been approved in cats, this drug has been used effectively in exotic felids at 0.03 to 0.1 mg/kg PO three times a week or up to every 48 hr (Whiteside et al., 2004; Plumb, 2005). Because studies have shown side effects like gastrointestinal ulceration at higher doses (European product, 2002), close monitoring of the patient is recommended. Carprofen is recommended to use as a single intra-operative dose of 4 mg/kg in domestic cats and can be given to exotic felids at a dose of 2 to 4 mg/kg IM, IV or PO. Ketoprofen is not as COX-2 specific compared with meloxicam and carprofen, but has been shown good analgesic properties in the domestic cat for years with well documented pharmacokinetics (Lees et al., 2003). The dose is 1.5 to 2 mg/kg IM, IV or SC (Galloway et al., 2002). Etodolac and tolfenamic acid have been used anecdotally in exotic felids, but their use must be done with caution because of lack of pharmacokinetic and pharmacodynamic studies. Both drugs are not licensed in cats.

Other Analgesic Agents

Ketamine is an N-methyl-D-aspartate (NMDA) antagonist, and provides analgesia at subanesthetic doses. If ketamine was not part of the induction protocol, it can be used as a CRI during the anesthetic procedure to provide supplemental analgesia when given at a loading bolus of 0.5 to 2 mg/kg and a CRI of 10 to 40 mcg/kg per minute. At the end of the procedure, the ketamine CRI should be titrated down to 3 to 5 μ g/kg per minute and stopped before the animal wakes up. If ketamine was used as part of the induction protocol, a loading bolus is not necessary and the CRI can be started after a catheter is placed.

 $\alpha_2\text{-}Adrenoceptor\ Agonists}$ The $\alpha_2\text{-}agonists$ provide excellent analgesia, but are accompanied by heavy sedation and serious cardiovascular side effects. When these drugs are part of the induction protocol in exotic felids, they provide some analgesia during the procedure, but it is important to realize that the analgesic effect will be eliminated when the drug is reversed. The synergism between opioids and $\alpha_2\text{-}receptor$ agonists has been well documented, and a combination of both groups of drug may be considered in certain cases.

Local Anesthesia

Local analgesia is advantageous to use because it reduces the systemic anesthetic requirements while providing concentrated analgesia and anesthesia to a specific anatomical area. Although commonly performed in small animal practices, it is often underused in zoo and exotic practice.

Infiltration anesthesia (diffuse infiltration of the operative area) and regional anesthesia (linear or incisional blocks, ring blocks) are very effective, low cost, and relatively simple ways of providing supplemental analgesia (Lemke and Dawson, 2000).

Local Blocks: Head Traumatic injuries to the teeth are common in captive felids. Local blocks around the head can be useful for tooth extraction or endodontic treatment (Van Foreest, 1993). In smaller cat species, a total of 0.1 to 0.3 ml of 2% lidocaine or 0.5% bupivacaine is needed to block the different facial nerves while in bigger species 1 to 3 ml may be required (Lemke and Dawson, 2000).

The infraorbital nerve block is used for analgesia of the rostral part of the upper dental arcade, soft and hard palate, nose, and muzzle. A needle is advanced into the infraorbital foramen and lidocaine or bupivacaine is injected. The infraorbital foramen usually can be palpated either intra-orally or extra-orally (Figure 39.5A).

The inferior alveolar nerve block provides analgesia to the lower dental arcade and the chin. This nerve can be blocked in two locations (proximally in the mandibular foramen or distally around the mental

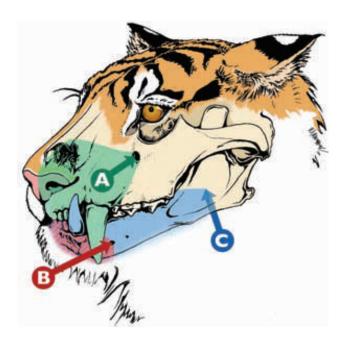


Figure 39.5. Drawing representing the local anesthetic blocks locations in the head. **A.** Infraorbital nerve block. **B.** Inferior alveolar nerve block (or mental nerve block). **C.** Mandibular nerve block. (Drawing courtesy of Michelle Mehalick, College of Veterinary Medicine, North Carolina State University.)

foramina). Both techniques are easy to perform (Lemke and Dawson, 2000) (Figure 39.5B,C). Blocking the nerve at the mental foramen will only block the lower incisors and chin. The mental foramen is located at the level of the second premolar and is easily palpated (Figure 39.5B). With the mandibular block the entire lower dental arcade is blocked. The landmark for placement of this block is the most ventral angle of the mandible and the needle is advanced along the medial surface of the mandible to the mandibular foramen (Figure 39.5C).

Occasionally ophthalmic procedures are done in exotic cats and, owing to the fact that Elizabethan collars are rarely an option, analgesia may prevent selfmutilation and scratching of the eye area. Topical analgesics such as prilocaine drops can be administered onto the cornea and provide analgesia for 2 to 3 hours. In a case of enucleation, a retrobulbar nerve block can be performed to block the ophthalmic nerve. This technique involves passing an appropriately sized precurved needle between the ocular globe and orbit, around the eye, until the caudal aspect of the globe is reached. Blocking the ophthalmic nerve anesthetizes the eye, orbit, conjunctiva, eyelids, and forehead skin and is performed with the needle placed at the orbital fissure. The ophthalmic block can also be done by placing the needle immediately below the zygomatic arch at the level of the lateral canthus and directing it in caudomedial direction toward the ear on the opposite side of the head. Via this technique the risk of direct subarachnoid injection, intravascular injection, and systemic absorption is decreased compares to the retrobulbar block.

For external ear injuries or procedures around the ear the auriculotemporal nerve can be blocked. The site of injection is rostral and caudal to the vertical ear canal, blocking the auriculotemporal nerve and the greater auricular nerve, respectively.

An epidural injection provides analgesia and local anesthesia to the caudal abdomen, hind legs, and tail area. The technique for exotic felid species is identical to that in domestic cats and placed in the intervertebral space between L7 and S1. Preservative-free morphine (0.1-0.3 mg/kg) and bupivacaine (1 ml/5 kg or 0.3 mg/kg, not exceeding 6-9 ml) are injected into the epidural space in the lumbosacral junction as described extensively elsewhere (Torske and Dyson, 2000). The analgesic effect usually lasts 8 to 12 hours, the local anesthetic effects will last between 1 and 4 hours depending on the local anesthetic selected. Epidurals have been used successfully in exotic felids for fracture repair with no side effects or behavioral changes observed postoperatively. The dose of drugs should be reduced if the subarachnoid is inadvertently punctured (the spinal cord and the dural sac ends further caudally in cats). For abdominal, thoracic or front leg analgesia, an epidural with morphine (0.1-0.3 mg/kg) and saline (total volume of 1 ml/4.5 kg) is used.

A brachial plexus block will provide analgesia to the foreleg distal to and including the elbow joint, but is rarely used in exotic practice because of fear to motor dysfunction of the leg post-operatively. With the use of a nerve finder, the risk for accidental injection into the nerve itself leading to nerve-damage and prolonged loss of motor function is minimized. To perform this block the leg is abducted from the body wall and the needle is placed at a point just proximal to the point of the elbow and advanced medial to the axilla toward the midscapula region until just caudal to the first rib. Doses for brachial plexus blocks are 1 ml/5 kg of 2% lidocaine or 1 ml/5 kg of 0.5% bupivacaine. An alternative technique

is the "high brachial plexus block," which is performed more proximal at the spinal canal (Lemke and Dawson, 2000).

The distal or "three-point-block" block of the superficial branches of the radius and median nerves and the dorsal and palmar branch of the ulnar nerve can provide good analgesia for toe amputations, onychectomy, etc. The radial nerve is blocked by injecting local anesthetic subcutaneously on the dorsomedial surface of the carpus just proximal to the joint. Infiltrating local anesthetic on either side of the carpal pad will block the palmar and dorsal branches of the ulnar nerve as well as the median nerve (Lemke and Dawson, 2000).

Table 39.1. Drug dosages for various felid species.

Drug		Dosage		Species
Ketamine + medetomidine	Ket	Meda		
	3	30		Large felids authors' recommendation
	1.9–5.7	18-80		Large felids: jaguars, leopards, lions, mountain lion, cheetahs. In tigers, use the lower a ₂ dosag to reduce cardiorespiratory effects
	2.5-4.5	50-70		Small felids: Asian golden cats, jungle cats, lynxes Pallas cats
Ketamine + medetomidine +	Ket	Meda	But	
butorphanol	0.8 - 2.5	37-57	0.15 - 0.2	Servals, Pallas cats
Ketamine + medetomidine +	Ket	Meda	Mid	
midazolam	1.5 - 2.5	30-50	0.1	Siberian tigers, lions
Ketamine + xylazine	Ket	Xyl		
•	3.5-6.8	0.3-1		Most species
	8	1-4		Wild lions
	20-30	1.5-2.3		Clouded leopards + other
Ketamine + xylazine + midazolam	Ket	Xyl	Mid	•
•	10	0.5	0.1	Siberian tigers
Ketamine-midazolam	Ket	Mid		Ŭ
	5-10	0.1-0.3		
Ketamine + midazolam + butorpha	nol Ket	Mid	Mid	
-	3-5	0.1-0.3	0.1 - 0.4	
Tiletamine-zolazepam	TZ			NOT RECOMMENDED TO USE IN TIGERS
_	1.6 - 4.2			Large felids recommendation
	3–5			Small felids recommend: black foots, fishing cats, Goeffrey cats, Iberian lynxes, lynxes, European lynxes, servals, bobcats
	4-8			Snow leopards, lions, leopards, wild jaguars, captive bobcats, Florida panthers
	6–11			Wild bobcats, jaguarundi, mountain lions, wild caracals
Tiletamine–zolazepam +	TZ	Meda		
Medetomidine	1.0 - 1.5	15-30		African lions + cheetahs
Tiletamine–zolazepam +	TZ	Ket	Xyl	
ketamine + xylazine	1.15 - 2	1.6-1.8	0.4-0.45	Cheetahs
Medetomidine-butorphanol-	Med	But	Mid	
midazolam	35	0.2	0.15	Cheetahs, lions = short length of anesthesia, sudden recoveries
Alphaxalone–alphadolone	AX	AD		
Propofol	1.4-2.5 IV P	0.45-0.85 IV		Cheetahs
	Maintenance	$e = 0.5-1 \text{ mg/kg I}^{\circ}$ 0.2 mg/kg/min IV	V every 5–10 m	in

All drugs given IM except alphadolone and propofol, which are IV.

 $[^]a$ All dosages are in mg/kg except for medetomidine, which is in μ g/kg.

AD, alphadolone; AX, alphaxalone; But, butorphanol; Ket, ketamine; Med, medetomidine; Mid, midazolam; P, propofol; TZ, tiletamine–zolazepam; Xyl, xylazine.

RECOVERY

When the procedure is finished, the animal ideally should be placed in a dark crate or a small dark room. The animal can be placed in ventral or lateral recumbency, with the head extended and closest to the door. It is important to realize that if the animal was maintained on one side during the procedure and was not intubated, it should be recovered on the same side down, as to keep the atelectic lung side down and the ventilated side up. If the animal was intubated, extubation should be done after the first swallowing occurs; however, some animals are extubated earlier for safety reasons. Cats generally swallow late and the ear-twitch reflex or obvious eye movements are taken as a sign for extubation. The endotracheal tube should be placed in a manner that the cuff or strings can not be caught on teeth or tongue when it is removed. Long tapes or strings can be used to pull the tube either through the bars or further away from the teeth of the animal. Because of safety reasons, intervention during recovery is usually not feasible. The animal should be released back within its group when fully awake or when the physical status of the animal allows (for example, after recovered from major procedures). Food and water can be offered a few hours after recovery. Corneal drying may occur because the eyes remain open and a bland ophthalmic ointment should be applied. Recovery time varies based on the drug type and dosage, species, duration of anesthesia, body temperature, disease status, and individual variation. In general, tiletamine-zolazepam recoveries are slow, the animal is sluggish for several hours, and can also be stormy. With ketamine and α_2 -agonists combinations, recovery time is generally much quicker due to the partial reversal of the α_2 -agonists, and felids are usually fully recovered within 1 hour. Gas anesthesia has a quicker recovery, usually less than 30 minutes. Fully reversible combinations are still experimental, but clinical evaluation showed extremely fast recoveries (Lafortune et al., 2005; Citino, personal communication, 2006).

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Phocid Seals

Michael Lynch and Kate Bodley

INTRODUCTION

Seals, sea lions, fur seals, and walruses make up a distinctive group of mammals: the order Pinnipedia. Most members of this group can be divided into two families: the Otariidae (eared seals) contains 14 species, and the Phocidae (true seals) contains 18 species (Riedman, 1990).

Phocid and otariid seals share many adaptive features that enable them to occupy both aquatic and terrestrial environments. However, there are significant anatomical, physiological, and behavioral variations among these groups and among species within each group. Some of these variations must be taken into account during the planning and management of immobilization and anesthesia procedures.

PRE-ANESTHETIC CONSIDERATIONS

Planning

When planning an immobilization procedure, the objectives must be clearly defined. This clarifies whether animal restraint is needed and if it is necessary, the degree of immobilization required. The method of immobilization must account for the animal's size, demeanor, and location.

Translocation without Restraint

It is possible to herd many phocid seals into trailers or transport crates using baffle boards and funneling arrangements. This is most applicable for captive animals. In the field, this technique may be suitable for species that are relatively tolerant of human disturbance, such as Weddell and southern elephant seals. Crates used to transport seals should be able to be opened at either end, well ventilated, and of a width and height that does not allow an animal to turn around and become trapped.

Physical Restraint

Minimally invasive procedures of short duration are most simply and safely achieved using physical restraint. Phocid seals less than or equal to 100 kg may either be cornered and manually restrained, or caught using a hoop net or pole noose. Manual restraint is achieved by grasping the animal's neck just behind the skull, and pushing it down to the ground while straddling the body. Depending on size of the seal, one or more personnel may be required to restrain the rest of the body.

Elusive species are difficult to approach on land. Harbor seals can be caught in narrow water canals using fine drift nets. Entangled animals are then hauled into a boat (M. Haulena, personal communication). Ringed seals are captured at breathing holes in sea ice using nets to line the hole (Kelly, 1996). Seals surfacing to breathe will trigger the fall of a weight that causes the net to extend. Larger phocids (e.g., crabeater, leopard, and southern elephant seals) are captured using a head bag (Stirling, 1966; Shaughnessy, 1991; Phelan and Green, 1992; McMahon et al., 2000; Kusagaya and Sato, 2001; Field et al., 2002). Once the head bag is in position, the animal is manually restrained with one person straddling the shoulders and another the hindquarters. A third handler can then perform minor procedures, such as blood collection and flipper tagging.

A major advantage of physical restraint is that the animal can be immediately released on completion of the procedure without residual drug effects that might impair its behavior. Physical restraint is used to facilitate accurate delivery of immobilization agents after the animal is caught. Southern elephant seals that received anesthetic agents IV after physical restraint had shorter induction and recovery times and less variable responses than those that were given the same agents by IM injection (Slip and Woods, 1996). Alternatively, animals are sedated via IM injection of chemical agents

prior to physical restraint for IV access (Woods et al., 1994a).

Disadvantages of physical restraint include increased risk for the handlers (e.g., bite wounds), animal stress, and the difficulty of adequately monitoring the animal's physiological status. Excessively vigorous restraint compromises breathing by occluding the airway or compressing the pliable thoracic wall.

Chemical Restraint

Remote injection either by dart (Higgins et al., 2002; Tahmindjis et al., 2003) or a needle attached to extension tubing (Ryding, 1982; Bodley, van Polanen Petel, and Gales, 2005) delivers drugs while minimizing animal disturbance. This reduces the risk of the handler being bitten. Drug delivery by dart is useful for large and potentially dangerous species (e.g., leopard seal) or species that become agitated or flee when approached by humans (e.g., crabeater seal). Once the animal is chemically restrained, anesthesia is induced or maintained using IV administration of parenteral drugs or inhalant anesthesia.

There are a number of advantages of using inhalant anesthetics for induction and maintenance. Inhalation anesthesia enables precise control of the animal's depth and gives the anesthetist control of the animal's airway. It is being used more frequently for field anesthesia of phocids because of the development of portable units that can be used under a wide variety of climatic conditions (Bodley, von Polanen, and Gales, 2005; Gales et al., 2005).

Immobilization Location There are many features in the captive environment that can be modified to achieve safe and effective chemical immobilization. For example, trained behaviors may allow venipuncture and IV administration of sedatives or anesthetics with minimal restraint. Facilities that allow rapid and safe restraint, restriction of access to water, and control of environmental factors such as temperature and animal interactions will simplify immobilization procedures and improve handler and animal safety.

In contrast, free-living phocids occupy a variety of habitats. Many of these areas are difficult to access and the environmental conditions are challenging. For each species, the sex and age distribution of groups and the physiological status of animals vary depending on the time of the year. This seasonal variability is also observed in the interactions between animals and reactions to the presence of humans. A major consideration for most immobilization procedures of free-living phocids is assessment of the likelihood that the animal will flee to the water. This is particularly important when anesthetic drugs are delivered by remote injection, as sedated animals may drown. In this situation it is important to understand the animal's response to human interference, and carefully approach the animal to a

distance where the dart can be placed accurately. Ideally, the seal should not be aware of the approach of the operator. At the very least the aim is that the animal remains calm so that the likelihood of it fleeing to the water when darted is reduced.

Assessment of Physiological Status An assessment of the current physiological status of an animal should be made prior to any immobilization procedure. Most captive animals have a known medical history, many have a previous anesthetic history, and their current disease status can be readily assessed. It is often possible to weigh captive animals prior to immobilization and assess this in relation to their annual cycle of weight fluctuation. In free-living animals, pre-anesthetic assessment is limited to characteristics that are easily observed (e.g., body condition), combined with an evaluation of the likely physiological status.

Weight fluctuations are generally the result of deposition or utilization of blubber; lean body mass varies less dramatically. Blubber is less metabolically active than most other tissues; therefore, it is important that dosages of anesthetic drugs are used without total body mass being the sole guide. A significant inverse relationship between body condition and duration of anesthesia has been demonstrated in southern elephant seals given a single IV dose of a 1:1 mixture of tiletamine and zolazepam (McMahon et al., 2000; Field et al., 2002). These authors suggest lipophilic drugs distribute from the bloodstream into blubber more rapidly in fatter animals; therefore, anesthetic duration is shorter than in thinner animals given the same dosage. However, there may be prolonged drug effects in fatter animals owing to gradual passage from saturated sites (e.g., fat), where it is inactive, back into the plasma. Therefore, the time to complete recovery (as opposed to the duration of effective chemical immobilization) might be expected to be longer in fatter animals.

CHEMICAL IMMOBILIZATION DRUGS

Table 40.1 reviews drug regimens that have been used in phocid seals.

Ketamine

Ketamine has been commonly used for immobilization (Gales, 1989) alone or in combination with other drugs. It has the advantage in phocids of causing minimal cardiopulmonary depression over a relatively wide dosage range. Northern elephant seals were immobilized using IM ketamine (1.4–6.9 mg/kg) (Briggs, Henrickson, and LeBoeuf, 1975), whereas it has been used IV (0.5–7.5 mg/kg) to successfully immobilize young Harp seals (Engelhardt, 1977). Adverse effects of ketamine alone include poor muscle relaxation and tremors (Briggs, Henrickson, and LeBoeuf, 1975). Therefore, it is used in combination with other drugs such as benzodiazepines

Table 40.1. Some immobilizing agents used in phocid seals.

Species	Agent and Dose Rate	Comments	Reference
Gray seal Halichoerus grypus	Tiletamine with zolazepam 1 mg/kg IM	Considered reliable and safe; however, some animals required ventilation.	Baker et al., 1990
	Tiletamine with zolazepam 0.5 mg/kg IM	Anesthesia for electroejaculation. Additional IM doses were required in some animals.	Lawson et al., 1996
	Medetomidine 60 µg/kg IM, followed 15 minutes later by ketamine 2 mg/kg IM	Apnea and bradycardia often occur; IPPV and careful cardiac monitoring required. Atipamezole used to reverse medetomidine.	Barnett, 1998
Leopard seal Hydrurga leptonyx	Tiletamine with zolazepam 2 mg/kg IM	Apnea, bradycardia, mortalities - seals were not intubated/ventilated during the study.	Mitchell and Burton, 1991
	Xylazine 0.8–2.8 mg/kg IM	Variable plane of anesthesia with lower dose, mortalities with higher dose.	Mitchell and Burton, 1991
	Midazolam 0.18–0.27 mg/kg with meperidine 1.0–1.5 mg/kg IM	Unpredictable immobilization, poor airway maintenance.	Higgins et al., 2002
	Tiletamine with zolazepam 0.5–1.5 mg/kg IM	Dose rate 1.2–1.4 mg/kg IM gave the most reliable response.	Higgins et al., 2002
Weddell seal Leptonychotes weddellii	Ketamine 0.15–0.25 mg/kg IM, then halothane 1–4% inhaled	For physiological studies. Features of anesthesia not described.	Hurford et al., 1996
	Tiletamine with zolazepam 0.3–1.1 mg/kg IM	Depth of anesthesia variable. Some mortalities. A lack of chemical antagonists considered a disadvantage.	Phelan and Green, 1992
	Midazolam 0.3–0.5 mg/kg IM, then isoflurane 2.5–5.0% inhaled	Dose rate for midazolam based on estimated bodymass only.	Bodley et al., 2005
Crabeater seal Lobodon carcinophagus	Midazolam 0.15-0.4 mg/kg with meperidine 1-3 mg/kg IM	Degree of sedation was unpredictable. Additional ketamine (1.3–2.0 mg/kg IM or 1.0 mg/kg IV) was used in two seals. Reversed using naloxone and flumazenil.	Tahmindjis et al., 2003
	Midazolam 0.26–0.85 mg/kg IM, then isoflurane 1.0–5.0% inhaled	Purpose-built gas anesthetic machine for field use.	Gales et al., 2005
Northern elephant seal Mirounga angustirostris	Medetomidine 70–140 μg/kg with ketamine 2.5 mg/kg IM	Bradycardia, prolonged recovery, poor reversibility, variable plane of anesthesia.	Haulena and Heath, 2001 M. Haulena pers. comm.,
	Tiletamine with zolazepam 0.8 mg/kg IV	Atropine given routinely (0.02 mg/kg IV) at the time of induction. IV Zoletil provides 15 minutes anesthesia at a level sufficient for intubation. Can then supplement with isoflurane as required.	Dailey et al., 2002
Southern elephant seal Mirounga leonina	Ketamine 4.4–8.6 mg/kg with diazepam 0.04–0.13 mg/kg IM	Apnea with upper respiratory tract obstruction.	Slip and Woods, 1996
	Ketamine 2.7 mg/kg with xylazine 0.48 mg/kg IM	Apnea, tremors. Superior analgesia and skeletal muscle relaxation than other sedative combinations given in the study. Hyperthermia.	Woods et al., 1994a
	Ketamine 3.0 mg/kg with xylazine 0.5 mg/kg IM	Some apnea, this was treated using doxapram 2 mg/kg.	Woods et al., 1996b
	Medetomidine 13.0–27.0 μg/kg IM	Vomiting, hyperthermia, bradycardia, poor restraint.	Woods et al., 1996a
	Medetomidine 17.0 μg/kg with ketamine 1.9 mg/kg IM	Hyperthermia, inconsistent and unpredictable response, poor reversibility, bradycardia	Woods et al., 1996a
	Midazolam 0.04 mg/kg with mepiridine 2.25–3.55 mg/kg IM	Rapid recovery after naloxone or naltrexone administration.	Woods et al., 1994b
	Midazolam 0.04 mg/kg with mepiridine 2.25–3.55 mg/kg IM, followed by thiopentone 3.4 mg/kg IV	Good immobilization of five minutes duration (allowing intubation) after thiopentone.	Woods et al., 1994b
	Midazolam 0.04 mg/kg with mepiridine 4.0 mg/kg IM, followed by ketamine 1.5–2.3 mg/kg IV	Initial ketamine dose 2.3 mg/kg followed by incremental doses of 1.5 mg/kg ketamine IV to maintain immobilization for 1 hour.	Woods et al., 1994b
	Ketamine 2.7 mg/kg with midazolam 0.02 mg/kg IM	Midazolam is the preferred benzodiazepine.	Woods et al., 1994a

Table 40.1. (Continued)

Species	Agent and Dose Rate	Comments	Reference
	Tiletamine with zolazepam 1 mg/kg IM	Some animals became apneic, requiring ventilation	Baker et al., 1990
	Tiletamine with zolazepam 1.6–2.4 mg/kg IM	Prolonged apnea, muscle tremors, mortalities.	Mitchell and Burton, 1991
	Tiletamine with zolazepam 0.7–1.2 mg/kg IM	Apnea, tremors, possible hallucinations. Predictable effect; dose rate > 1.0 mg/kg associated with complications including fatalities.	Woods et al., 1994a
	Tiletamine with zolazepam 0.46 mg/kg IV	Satisfactory immobilization for gastric lavage and blood sampling.	McMahon et al., 2000
Harbor seal Phoca vitulina	Propofol 2.0–6.0 mg/kg IV	Optimal short-acting anesthetic when given at 5 mg/kg. Some apnea. All animals received atropine 0.02 mg/kg premedication.	Gulland et al., 1999
	Propofol 3.0–5.0 mg/kg IV, followed by isoflurane 2.0–5.0% inhaled	Optimal short-acting anesthetic when given at 5 mg/kg. Easily intubated, some apnea.	Gulland et al., 1999
	Butorphanol 0.4 mg/kg IM	Decreased anxiety, relaxation sufficient for minor procedures.	Tuomi et al., 2000
	Butorphanol 0.4 mg/kg IM, followed by diazepam 0.2 mg/kg IV	Immobilization sufficient for deep muscle biopsy, endoscopy	Tuomi et al., 2000
	Diazepam 0.15–0.2 mg/kg IV, followed by isoflurane 0.5–2.5% inhaled	Atropine is given routinely (0.02 mg/kg IV) at the time of induction.	M. Haulena pers. comm.
	Medetomidine 60 μg/kg IM, followed 15 minutes later by	Apnea and bradycardia often occur, IPPV and careful cardiac monitoring required.	Barnett, 1998
	ketamine 2.0 mg/kg IM Butorphanol 0.2 mg/kg IV, followed by isoflurane 1.5–5.0% inhaled	Atipamezole used to reverse medetomidine. Atropine is given routinely (0.02 mg/kg IV) at the time of induction.	M. Haulena pers. comm.

IM = intramuscular injection.

 $IV = intravenous \, injection. \,$

(e.g., diazepam or midazolam) or α_2 -agonists (e.g., xylazine, detomidine, or medetomidine).

Benzodiazepines

Benzodiazepines are very useful because of their muscle relaxant properties, minimal cardiovascular effects, and reversibility with specific antagonists. Prior to the introduction of midazolam, mixtures of ketamine and diazepam were commonly used to immobilize many phocid species (Table 40.1). Midazolam has several advantages over diazepam, including its unique solubility characteristics (water-soluble injection but lipid soluble at body pH) that produces a very rapid onset of action following injection (Plumb, 2005).

Benzodiazepines are used for premedication to facilitate safe physical restraint. Hawaiian Monk seals have been sedated using diazepam (0.15 mg/kg IM) prior to restraint for mask induction with isoflurane (Levine et al., 2005). Midazolam (0.15–0.2 mg/kg IM) produces moderate sedation (stage 1–2 sedation, Table 40.2), whereas higher dosages (0.4–0.5 mg/kg IM) produce heavy sedation (stage 2–3 sedation, Table 40.2). The higher dosages are useful for larger species, in which physical restraint in un-sedated animals is dangerous for handlers and stressful for the animal. Midazolam

 $(0.51 \pm 0.19 \text{ mg/kg IM})$ produces moderate sedation in crabeater seals (Gales et al., 2005). This level of sedation allowed restraint for anesthetic induction using isoflurane.

α₂-Adrenergic Agonists

Xylazine (alone and in combination with ketamine) has been used successfully (Table 40.1). Xylazine alone has been associated with hyperthermia, bradycardia, and high rates of mortality in leopard and southern elephant seals (Mitchell and Burton, 1991). Medetomidine/ ketamine in southern elephant seals produced similar undesirable side effects (Woods et al., 1996a). Generally, α₂-adrenergic agonists result in undesirable cardiovascular side effects, including decreased cardiac output, bradycardia, and increased peripheral vascular resistance. Prolonged anesthetic recovery, bradycardia, and variable levels of anesthesia have been observed in harbor and northern elephant seals following administration of medetomidine (M. Haulena, personal communication; Haulena and Heath, 2001). However, this drug has been routinely used by other authors to sedate harbor and grey seals, and combined with ketamine to induce anesthesia in these species (Barnett, 1998). The α_2 -adrenergic agonists offer the advantage of

Table 40.2. Stages of immobilization in phocid seals.

Stage	Description
0	No effect.
1	Negligible sedation.
2	Visibly sedated but mobile.
3	Sedated. Sluggish movement in response to body or head touch. Locomotion may be elicited with repeated stimulus.
	Hand injection possible.
4	Small movements of head or eyes. Locomotion possible but sluggish. Stage of immobilization sufficient if not adjacent to water.
5	No body movement. Muscle tone variable, dependent on drug used. Eye may follow passing objects.
6	No response to vigorous shaking of the tail, body, or head. Very little muscle tone. Sluggish palpebral response.
7	As for stage 6 but slightly deeper, with some respiratory depression and negligible muscle tone. Negligible palpebral response.
8	Deep anesthesia. Cardiac or respiratory depression. Complete loss of muscle tone. No palpebral response.

From Higgins DP, Rogers TL, Irvine A, et al. Use of midazolam/pethidine and tiletamine/zolazepam combinations for the chemical restraint of leopard seals (*Hydrurga leptonyx*). *Mar Mamm Sci* 2002;18:483–499.

reversibility using antagonists such as yohimbine and atipamezole.

Tiletamine/Zolazepam

A 1:1combination of tiletamine and zolazepam has been used in a wide range of phocids. As a fixed ratio combination it does not allow fine adjustments in the dosage of either agent to suit a particular species. This combination has been used in southern elephant seals both intramuscularly (IM, 1 mg/kg) (Woods et al., 1994a) and intravenously (IV, 0.5 mg/kg) (McMahon et al., 2000). Harbor seals have been anesthetized (0.8–1.2 mg/kg IV) after physical restraint (Dunker et al., 2001; Lander, Haulena, and Gulland, 2005), and a similar regimen has been described in northern elephant seals (Dailey, Haulena, and Lawrence, 2002). This combination (1 mg/kg IM) was also effective in immobilizing grey seals (Baker, Fedak, and Anderson, 1990). Conversely, tiletamine/zolazepam IM in 30 Weddell seals produced variable immobilization and six displayed prolonged apnea, with three eventually dying (Phelan and Green, 1992). Variable responses were also observed in leopard seals (1.2–1.4 mg/kg IM) (Higgins et al., 2002).

In general, IV tiletamine/zolazepam produces more predictable immobilization with fewer adverse side effects (e.g., prolonged apnea and muscle tremors) compared with IM administration. Response is also less predictable following delivery by remote delivery systems than following accurate deposition of drug in an optimal site (i.e., into the extradural vein or directly into the lumbar musculature).

Opioids

Anesthetic regimens that include opioids have been used (Table 40.1). There are several advantages of using opioids. They can be reversed using naloxone or naltrexone, and they usually have relatively mild cardiovascular and respiratory side effects when used at low dosages. A mixture of meperidine (pethidine) and midazolam in southern elephant seals induced a reliable deep sedation that allowed IV access for the administration of ketamine or thiopentone (Woods et al., 1994a). However,

meperidine/midazolam was unsatisfactory in leopard seals because of variable effect, respiratory depression, and loss of muscle tone that compromised airway patency (Higgins et al., 2002). This combination induces deep sedation and light anesthesia in crabeater seals (Tahmindjis et al., 2003), although periods of prolonged apnea were noted. Meperidine, when given as the sole sedative agent, produced moderate restraint without respiratory depression in harbor and northern elephant seals (Joseph and Cornell, 1988). Butorphanol tartrate (0.4 mg/kg IM) produced mild sedation (decreased anxiety during minor procedures) in harbor seals. The addition of diazepam (0.2 mg/kg IV) allowed more invasive procedures (muscle biopsy, endoscopy) to be performed (Tuomi, Grey, and Christen, 2000).

Potent opioids (i.e., etorphine and carfentanil) produced respiratory depression, hyperexcitability, and prolonged apnea in hooded and grey seals. Their only advantage is small drug volume delivery (Haigh and Stewart, 1979; Baker and Gatesman, 1985).

Propofol

Propofol (5 mg/kg IV) was evaluated in 12 harbor seal pups, two northern elephant seal pups, and two harbor seal adults (Gulland and Gage, 1997). It produced short-duration general anesthesia, good muscle relaxation, and rapid recoveries. Gulland et al. (1999) also showed that propofol (5 mg/kg IV) provided good anesthesia for brief procedures in 18 harbor seal pups. The primary disadvantage of this drug is the large volumes of the commercially available preparations (10 mg/ml) required for animals over 40 kg.

Inhalant Anesthetics

Prolonged immobilization procedures or those requiring a surgical plane of anesthesia are most safely performed using inhalant techniques. Studies in grey seals have demonstrated an efficient exchange of large volumes of gases during surface breathing, in part because the animals have a large tidal volume (Reed et al., 1994). This suggests diving seals achieve rapid and efficient uptake and distribution of inhalant anesthetics

(Haulena and Heath, 2001; Gales et al., 2005). The use of a precision vaporizer and anesthetic circuit allows accurate delivery of a known, clinically useful concentration of the inhalant in oxygen. Endotracheal intubation completes the anesthetic circuit and gives the anesthetist control over the animal's airway. Maintenance of a clear airway is particularly significant during anesthesia of phocid seals, as many of these species have reduced cartilaginous support of the trachea and so are prone to respiratory obstruction (Hammond and Elsner, 1977; Higgins et al., 2002). In addition, many species have a very fleshy pharyngeal region that contributes to respiratory obstruction when muscular tone is reduced by sedation (Phelan and Green, 1992). The most frequently used inhalant anesthetics in pinnipeds are halothane, isoflurane, and sevoflurane.

ANALGESIA

Phocid seals may require analgesia during periods of illness or following trauma or surgery. Use of both opioids and non-steroidal anti-inflammatory drugs (NSAIDs) has been reported. Nutter, Haulena, and Bai (1998) described pharmacokinetics of single-dose butorphanol in northern elephant seals, and determined a dosage 55 µg/kg IM resulted in detectable plasma levels for up to 5 hours postinjection, and produced sedation for up to 3 hours. The NSAID flunixin meglumine has been used to treat ocular inflammation in southern elephant seals (Vogelnest, Hulst, and Woods, 1996) and musculoskeletal disorders in grey and harbor seals (Barnett, 1998). Anorexia has been reported in southern elephant seals treated with flunixin meglumine for more than 72 hours, possibly the result of gastric inflammation/ulceration (Vogelnest, Hulst, and Woods, 1996; Barnett, 1998). The NSAIDs carprofen and meloxicam have been administered orally and IM, at canine dosages (Barnett, 1998; Lucas, Barnett, and Riley, 1999) without adverse effects.

RESPIRATORY STIMULANTS AND ANTAGONISTS

Doxapram increased the depth and frequency of respiration and stimulated breathing in apneic southern elephant seals (Woods et al., 1996b). It failed to stimulate breathing when delivered into the extradural sinus, but direct intratracheal administration (via an endotracheal tube) stimulated breathing in four of six apneic animals. The lack of efficacy of IV doxapram was probably owing to low pressures and flows in this vessel during breath holding. There have been no reported studies to determine whether the doxapram administration to hypoventilating phocid seals improves respiration and/or oxygen delivery to the tissues. Doxapram (5.0 mg/kg) was a nonspecific antagonist for ketamine-diazepam sedation in southern elephant seals, but often caused shaking and hyperresponsive animals, prompting a recommendation to use a lower dosage (Woods et al., 1995).

Antagonists potentially improve safety of chemical immobilization of pinnipeds: they may be used during emergency resuscitation and to reduce recovery times. Yohimbine (0.5 mg/kg IM) hastened recovery from ketamine-xylazine-diazepam sedation in Weddell seals (Bornemann and Plötz, 1993) and has also been used (0.06 mg/kg IV) to hasten recovery in southern elephant seals under ketamine-xylazine sedation (Woods et al., 1995). Low-dose atipamezole (median 0.04 mg/kg IV) failed to arouse southern elephant seals from ketamine-medetomidine anaesthesia (Woods et al., 1996b).

Flumazenil is a useful adjunct to anesthetic management of phocid seals immobilized with benzodiazepine combinations. In crabeater seals (250–300 kg) a combination of meperidine (1.29–2.2 mg/kg IM) and midazolam (0.29–0.37 mg/kg IM) was partially antagonized by naloxone (1.2–4 mg IV) and flumazenil (0.1–0.5) (M. Lynch). Although the time to recovery was greatly shortened, reversal of drug effects was not complete and higher dosages may be indicated. Flumazenil (1 mg per 20–25 mg benzodiazepine IM) has also been used to reverse the zolazepam in southern elephant seals immobilized with tiletamine-zolazepam (Karesh et al., 1997).

PHYSIOLOGICAL AND ANATOMICAL CONSIDERATIONS

Adaptations for Diving

Phocid seals are physiologically well adapted to dive deeply and for prolonged periods while foraging. There is a common belief that cardiopulmonary reflexes that occur during diving (the "dive response") may be elicited inappropriately during anesthesia, leading to death. The dive response is characterized by profound bradycardia, peripheral vasoconstriction, and shunting of blood to essential and hypoxia-sensitive tissues, such as the heart and brain (Scheffer, 1990). The pinniped dive response is primarily controlled by central mechanisms influencing respiratory drive and input from pulmonary stretch receptors, arterial chemoreceptors and baroreceptors, and trigeminal receptors elicit a vagally mediated bradycardia (Angell-James, Elsner, and de Burgh Daly, 1981). The activity of the sympathetic nervous system also increases, resulting in splenic contraction, peripheral vasoconstriction, and constriction of the muscular vena cava sphincter. Consequently, there is an increased hematocrit and pooling of blood within the hepatic sinus during diving (Thornton et al., 2001).

It is difficult to state with confidence that the profound bradycardia and periods of prolonged apnea observed in some anesthetized seals is owing to a dive response, as hypoxemia and bradycardia would be expected to result from significant apnea in any mammal. However, it is not unreasonable to imagine that the dive response could be elicited during anesthesia, as anesthetic drugs depress central respiratory and cardiovascular centers, and may induce periods of apnea.

Anesthesia may be considered as providing two of the triggers, central and peripheral, for elicitation of a dive response.

Atropine has been used at a wide variety of dosages (Gales and Burton, 1988; Mitchell and Burton, 1991). It is usually included in anesthetic regimens in an attempt to reverse some of the physiological effects of the dive response. Standard dosages (0.02-0.04 mg/kg) for terrestrial carnivores were used in un-sedated harbor seals to eliminate the reflex bradycardia that occurs during diving (Galantsev, Kovalenko, and Popov, 1984). It is likely that similar dosages would be effective in pinnipeds. However, it would be expected that atropinization would not affect the vasoconstriction and venous pooling. Although atropine is routinely included in anesthetic drug protocols, several authors do not routinely include it, without apparent adverse effects (McMahon et al., 2000; Kusagaya and Sato, 2001; Bodley, von Polanen, and Gales, 2005; Gales et al., 2005).

It is possible the mortalities attributed to initiation of the dive response were caused by hypoxemia induced by poor ventilation. The sudden bradycardia, apnea, and rapid death seen in these circumstances are consistent with clinical signs of hypoxia-induced cardiac arrest. Endotracheal intubation is strongly recommended to maintain the airway and the ability to ventilate the animal. Careful monitoring of the physiological status of anesthetized phocid seals, including the use of capnography, allows continuous assessment of respiratory function and reduces the risk of development of hypercapnia and hypoxemia.

Anatomical Considerations

Upper Airway In phocid seals the tracheal cartilage is incomplete and has a dorsoventrally flattened shape. In the Ross, leopard seal, and Weddell seals, tracheal anatomy allows complete collapse (Kooyman and Anderson, 1969). During anesthesia, relaxation of muscles supporting the trachea results in partial tracheal collapse, causing obstruction. Respiratory obstruction is very common in leopard seals, and is probably the major contributor to the high mortality associated with chemical immobilization in this species (Mitchell and Burton, 1991; Higgins et al., 2002).

Endotracheal Intubation and Ventilation Hypoventilation is also significant during phocid anesthesia. It is essential that both respiratory rate and tidal volume be continuously monitored. Haulena and Heath (2001) observed that ventilatory effort is reduced in anesthetized phocids. The anesthetist must be prepared to assist ventilation if hypoventilation is apparent (i.e., reduced thoracic excursions during breathing, increasing end-tidal CO_2 values).

Personnel performing chemical immobilization should have the capacity to intubate and ventilate animals. Intubation is required to ensure reliable maintenance of the airway during anesthesia. However, intubation may be difficult, particularly in larger animals. A number of authors describe the presence of spongy peripharyngeal tissues and a flaccid soft palate that prevent visualization of the laryngeal opening (Phelan and Green, 1992). Hammond and Elsner (1977) describe the narrow laryngeal orifice in Weddell seals. This narrowing makes it difficult to insert an endotracheal tube of a size suitable for the lumen of the trachea.

In larger phocid seals, intubation is most easily accomplished by manually palpating the laryngeal opening and then passing the tube. Laryngoscopes may be used for smaller species (less than or equal to 100 kg), but often do not displace enough pharyngeal tissue to visualize the glottal opening. A spatula of 5- to 8-cm width will aid this process (Haulena and Heath, 2001).

Glottal manipulation in apneic phocid seals often stimulates respiration. However, Woods et al. (1996b) observed apnea associated with endotracheal tube placement in 24 of 31 previously breathing, lightly anesthetized southern elephant seals. In most seals the apnea was resolved by tube removal alone.

For assisted ventilation, intubated large seals require oxygen demand valves capable of delivering high flow rates. A modified Robert-Shaw demand and resuscitation valve (Ohmeda, Madison, WI), capable of delivering an oxygen flow of 140 L/minute has been used by the authors to ventilate phocid seals less than or equal to 300 kg body weight. A device capable of delivering 300L/minute is described in a report by Horne, Tchamba, and Loomis (2001), and is capable of ventilating the very largest phocid seals.

Vascular Access The extradural intravertebral vein is frequently used for IV access. The vein is located dorsal to the spinal cord, in the epidural sinus (Figure 40.1). The animal is restrained in sternal recumbency and the vein is located by determining the dorsal midline in the lower lumbar region. The spinous processes of lumbar vertebrae 3 to 4 are located by palpation and the needle is inserted perpendicularly between these processes until blood is observed in the needle hub (McMahon et al., 2000; Haulena and Heath, 2001). A 20-g, 2.5-cm (1-in.) needle has been recommended for harbor seal pups, an 18-g, 7.6-cm (3-in.) spinal needle for harbor seal adults, and an 18-g, 9.0-cm (3.5-in.) spinal needle for southern elephant seal adults (McMahon et al., 2000; Haulena and Heath, 2001). If extradural intravertebral venipuncture is performed without adequate skin preparation, there is the potential for introduction of pathogens directly into a major vessel (Slip and Woods, 1996). Care must be taken when attempting IV access in a restrained seal: If the animal struggles, there is the potential for vessel trauma (Slip and Woods, 1996). Inadvertent bone marrow contamination of blood samples has been reported during extradural intravertebral vein access in northern elephant seal pups (Goldstein et al., 1998).

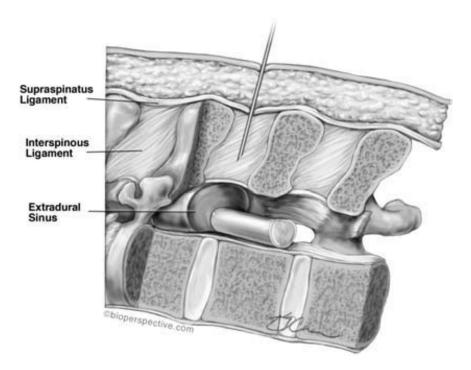


Figure 40.1. A schematic diagram of a sagittal section of the lower lumbar region of a phocid seal demonstrating the perpendicular placement of a needle to enter the extradural sinus.

The plantar interdigital veins of the hind flippers have also been used for IV access. A needle is inserted at the origin of the interdigital webbing, 10 to 20 degrees to the skin surface directly over the second digit or medial to the fourth digit (Gulland, Haulena, and Dierauf, 2001). Firm pressure must be applied to this site post-venipuncture to prevent hematoma formation.

MONITORING

The plane of sedation or anesthesia is determined using basic responses such as the ability to move the body, head and flipper movements, jaw tone, and palpebral reflexes (Woods et al., 1994a). Table 40.2 defines levels of chemical restraint observed in leopard seals according to Higgins et al. (2002).

The assessment of physiological variables is essential for the safe management of any chemical immobilization procedure. The animal's heart rate is continuously monitored, so bradycardia, whether from hypoxemia or presumed dive response, is quickly detected and treatment instituted immediately. It is difficult to auscultate the heart through the thoracic wall and an esophageal stethoscope should be used. Alternatively, the heart rate is counted by the visualization of movements of the thoracic wall. Monitoring devices with electrocardiographic capacity are useful for assessment of the rate and rhythm. However, their deployment in field situations can be difficult.

Prolonged apnea is common (Haulena and Heath, 2001). However, the respiratory pattern in sleeping



Figure 40.2. Monitoring end-tidal carbon dioxide levels and hemoglobin saturation with a capnometer and pulse oximeter, respectively, in an intubated, anesthetized leopard seal. The pulse oximeter probe is placed on the tongue, and the capnometer is attached to the end of the endotracheal tube.

phocid seals is characterized by frequent periods of apnea (Castellini et al., 1994). Because anesthetic agents often produce changes in the cardiovascular and respiratory systems, direct time comparisons between these events should be interpreted with caution. The determination of what is a life-threatening duration of apnea is species dependent and related to their aerobic dive capacity (Slip and Woods, 1996). The aerobic dive limit (ADL) is defined as the time beyond which an animal must rely on anaerobic metabolism to prolong the dive

(Kooyman, Castellini, and Davis, 1981). Species that are capable of deep and prolonged dives (e.g., southern elephant and Weddell seals) have a greater ADL and would be expected to tolerate longer periods of apnea under anesthesia compared with shallow diving species. Ultimately, respiratory rates and periods of apnea in anesthetized phocid seals should be interpreted in light of the other physiological variables that reflect ventilation and perfusion.

In addition to visualization of mucous membrane color, determination of hemoglobin saturation with pulse oximetry is a valuable aid when assessing ventilation and perfusion. Probe placement sites include the vulva, lip, and tongue (Figure 40.2). Capnography is also an extremely useful tool for assessing adequacy of ventilation. To obtain accurate ETCO₂ readings the animal must be intubated. There are no published normal values for this variable in anesthetized phocid seals, but it is the authors' belief that assisted ventilation is indicated when ETCO₂ exceeds 55 mmHg. This figure is based in part on the authors' observations of ETCO₂ values during the initial period of anesthetic procedures on both otariid seals and phocid seals, and in part on experimental studies. Parkos and Wahrenbrock (1987) found the ventilatory response to hypercapnia in unanesthetized Weddell seals did not differ from that of terrestrial mammals. Reed et al. (1994) measured ETCO2 values in freely diving grey seals and found they ranged between 28 and 35 mmHg, a range not dissimilar to that seen in terrestrial mammals. Non-invasive blood pressure monitoring is not applicable because of the lack of readily accessible peripheral arteries.

Anesthetic agents disrupt the ability of phocid seals to thermoregulate. Seals in cold environments given vasodilatory agents may become hypothermic (Hammond and Elsner, 1977), probably because of disruption of their counter-current heat exchange mechanisms. Behavioral thermoregulation will also be affected by immobilization (Gales, 1989), resulting in hyperthermia. In temperate or warmer climates, seals recovering from anesthesia are kept wet and/or in the shade. Accurate measurement of body temperature in larger phocid seals requires rectal temperature probes of at least 30 cm in length (Phelan and Green, 1992).

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41

Otariid Seals

Martin Haulena

INTRODUCTION

The family Otariidae (sea lions and fur seals) within the order Pinnipedia is composed of 14 species. Otariids bear weight on all four flippers, climb, locomote quickly, and are more adept on land than phocid seals. However, their aquatic adaptations are less developed and they generally do not dive as deep or for as long as phocids. Anatomical and physiological adaptations for diving (e.g., large venous sinuses and dive response) therefore, are not as extreme (Elsner, 1999; Pabst, Rommel, and McLellan, 1999). Some of these differences make otariids more difficult to physically or mechanically restrain than phocids of the same weight. Additionally, they are less sensitive to immobilization drugs and anesthetic regimens are similar to those of terrestrial carnivores.

PRE-ANESTHETIC CONSIDERATIONS

Planning

As with any species, successful otariid anesthesia is dependent upon adequate planning and availability of the proper equipment. The animal's size, species, sex, and physiological status are important considerations in choosing the best immobilization method. The site (captive facility versus free-living animals in the field), experience of the personnel, and availability of equipment and drugs often dictate the method chosen. Finally, the degree of invasiveness and expected duration of the procedure affect decisions.

Translocation without Restraint

Many otariid species are easily trained to follow trainers, and voluntarily enter different housing units or transport cages. Training of permanent captives is essential for enrichment, minimizing stress and facilitating medical procedures. Animals captive for only short periods of time, as in a wildlife rehabilitation center or research

facility, require the use of protective equipment by handlers. Depending on size and species, animals can be safely moved with herding boards, chutes, and mobile fencing. They can be herded into cages or transport containers for longer travel. Free-living pups from a variety of species are safely herded into temporary corrals using long poles. Depending on the local topography, moving healthy adult otariids is very challenging and requires well-trained, experienced personnel.

Physical Restraint

Physical restraint is primarily limited by the animal's size and the experience of personnel. Training captive animals for a variety of behaviors minimizes the requirement for physical restraint. Towels, protective gloves, or sedative drugs may facilitate restraint.

Multiple personnel are required to restrain animals greater than or equal to 20 kg. Mechanical or drug assisted restraint is strongly recommended for healthy untrained animals greater than or equal to 90 kg. Larger debilitated animals, such as those encountered at rehabilitation centers, may be restrained using only physical methods. The limitations of physical restraint in otarids include short allowable duration of procedures, poor accessibility to various parts of the animal, lack of analgesia, risk of injury to personnel, and undue stress to the animal as a result of prolonged struggling.

Otariids are quick, agile, and strong and use their large carnivorous teeth in defense. Controlling the head is essential. Sea lions have tremendous power in their forelimb muscles. If they gain a purchase, and are able to lift their thorax off the ground, they will easily throw off a person. Care is taken to control the front flippers, raising them slightly and holding them against the side of the animal. This is particularly important in animals greater than or equal to 20 kg. Animal safety concerns include ensuring airway integrity and the head is not turned at an awkward angle or held over an edge that may collapse the trachea. Too much weight on the

thorax inhibits ventilation. Musculoskeletal problems arise from excessive restraint on the extremities. Care must be taken to avoid soft-tissue injuries, including abrasions and scrapes, if restraint is on a rough substrate.

Mechanically Assisted Restraint

There are several commercially available large carnivore squeeze cages that have been used successfully in a variety of otariid species. Although many designs exist, squeeze cages that entrap the animal's neck in a vise or noose put pressure on the trachea and should be avoided. The otariid trachea easily collapses because of incomplete tracheal rings. When using squeeze cages, it is important to closely monitor the respiratory excursions and mucous membrane color of the animal. Care is taken to avoid pinching extremities, especially as the cage begins to squeeze. The cage bars may be padded to avoid soft-tissue injury. Biting the bars results in tooth fracture and should be avoided. Captive animals can be trained to enter a cage and be squeezed to allow sample collection (e.g., for venipuncture). Some animals have been trained to accept delivery of an anesthetic gas through a mask without further restraint. As with physical restraint, sedative agents may decrease the degree of struggling and facilitate restraint.

There are a variety of commercially available nets custom-designed for use in otariids. Nets aid in capturing animals, can be used for restraint, and facilitate administration of chemical immobilization drugs. Welldesigned nets are somewhat tubular to keep the pectoral limbs against the side and prevent the animal from lifting itself up. Nets should be wide enough to easily capture the animal, but taper to a point so the head can be easily controlled. In the field, care must be taken to monitor an animal in a net for hyperthermia and exhaustion after capture. Animals have overheated in tightly fitting nets left in the sun while other animals are being sampled or processed. Some nets have small openings at the tip that allow exposure of the nares and rostrum but are tight enough to prevent the animal from biting personnel. These openings aid in masking an animal with an inhalant anesthetic after capture.

Recently, a method of capturing free-ranging Steller sea lions (*Eumetopias jubatus*) in the water was developed using a team of divers, baited nooses attached to floats, and a surface capture team in boats (Raum-Suryan et al., 2004). This capture method requires a tremendous amount of training and planning and should only be carried out by highly experienced staff.

Although most methods of mechanical restraint enhance safety for personnel, training and experience are required to ensure adequate and safe restraint. Most mechanical devices, including nets, limit access to the animal for some procedures.

Chemical Restraint

Venous access in many species is difficult to maintain for intravenous (IV) injection. This is particularly true for difficult to restrain animals and under field conditions (Work et al., 1993). Most anesthetic drugs evaluated for use, therefore, have been limited to those that can be administered IM (Bester, 1988; Loughlin and Spraker, 1989; Heard and Beusse, 1993; Heath et al., 1996) and inhalant anesthetics (Work et al., 1993; Heath et al., 1997; Yamaya et al., 2006).

Intramuscular drugs are injected into the large muscle masses overlying the lower lumbar spine (Bester, 1988; Loughlin and Spraker, 1989), tibia and hips (Loughlin and Spraker, 1989; Heard and Beusse, 1993; Sepulveda, Ochua-Acuna, and McLaughlin, 1994; Haulena et al., 2000) as well as the shoulders (Loughlin and Spraker, 1989). Immobilizing intramuscular (IM) agents have been hand-injected or delivered by dart. Physical or mechanical restraint may facilitate accurate hand injection of anesthetic agents. Delivery by dart has been used in captive animals (Haulena et al., 2000) as well as in the field (Heath et al., 1996). In free-living animals, delivery by dart poses some risk to animals that may escape to the water or an inaccessible area as the anesthetic drug begins to take effect prior to complete immobilization (Heath et al., 1996). Some authors report a decrease in the reliability of anesthesia when darts are employed, in comparison to hand injection (Haulena et al., 2000).

Inhalation anesthetics (e.g., isoflurane) appear to be the safest method for anesthetizing otariids because of the ability to titrate the level of drug to effect. The main limitation is the availability and portability of equipment to safely and reliably deliver the anesthetic in the field. In addition, delivery of a gas for a sufficient period of time to induce anesthesia may be difficult in a fractious, unrestrained animal. Most public display facilities, rehabilitation centers, and research facilities are equipped for delivery of inhalant anesthetics. A recent publication describes the use of an induction chamber for delivery of inhalant anesthesia to sea lions (Yamaya et al., 2006). The development of safe, portable gas anesthesia machines for field work has greatly increased the use of gas anesthesia in free-living species. A comprehensive animal training program, adequate physical or mechanical restraint, or the use of chemical sedative and immobilizing agents (Heard and Beusse, 1993; Heath et al., 1996; Haulena et al., 2000; Haulena and Gulland, 2001) facilitates the use of inhalation anesthesia.

Although chemical immobilization is the safest method of restraint for personnel, allowing complete access to the entire animal, there is some risk to the animal being anesthetized. This risk is minimized by adequate preparation, use of experienced anesthetists, use of safe and efficacious immobilization agents, careful monitoring, and physiological support of the animal.

Immobilization Location

As with phocid seals, otariid immobilization success is greatly enhanced by good planning, proper equipment, experienced staff, and a well-prepared space. The ability

to safely handle, restrain, and deliver anesthetic agents to the animal is essential. A surgery or procedure area that includes an accessible immobilization and recovery pen for monitoring or emergencies is recommended. The ability to control temperature, noise, and light will help induction and physiological support of the patient. Immobilization of larger animals may that require procedures be carried out in the animal's pen because of space and transport limitations. Adequate pre-procedure planning and availability of emergency equipment are essential for a safe procedure.

Immobilization of animals in the field presents significant challenges. However, portable gas anesthesia machines, battery-operated monitoring equipment, and emergency equipment are all available (Gales and Mattlin, 1998). If injectable chemical immobilization is required prior to adequate physical or mechanical restraint, it is essential that animals selected for capture are as far as possible from water or other hazards. It is also important to choose animals that are relatively calm and have the least risk of escaping into the water or inaccessible areas (Heath et al., 1996). This will help minimize the risk of drowning or falling from large heights.

Assessment of Physiological Status

Pre-anesthetic assessment is important for selection of the optimal method of immobilization and to decrease the incidence of adverse side effects. It is often very difficult to obtain a complete medical history for an individual animal, particularly for free-living animals or those undergoing rehabilitation. A medical history for captive animals may be available. However, even for these animals, the purpose of the immobilization procedure may be to gather information and samples to diagnose an unknown condition. Therefore, it is important to try to select animals that are in good body condition and of known health status for elective procedures or for field studies. In addition, it is important to have some knowledge of the common medical conditions that affect both captive and free-living animals in order to facilitate pre-procedure planning.

Some problems are specific to species, sex, age, season, or geographic location. For example, most stranded animals entering a rehabilitation program are dehydrated, malnourished, and may have infectious disease conditions that should be stabilized prior to an anesthetic procedure. Particular attention to these potential problems will lead to better intra-procedure physiological support. Free-living animals, particularly juveniles, may have high parasite loads. Parasitic pneumonia caused by Parafilaroides decorus in species such as the California sea lion (Zalophus californianus) (Gage et al., 1993) may exacerbate ventilation problems encountered during an anesthetic procedure. Young animals such as northern fur seals (Callorhinus ursinus) may be affected by hookworm (*Uncinaria* sp.), which can cause anemia (Lyons et al., 2000). These animals are prone to

hypoxemia and vascular compromise. Dehydrated juvenile and subadult California sea lions stranded during the late summer and early fall are often affected by leptospirosis, which may cause renal failure (Gulland et al., 1996). Poor renal function can significantly alter the excretion of some parenteral anesthetics. Animals with clinical leptospirosis are poor anesthetic candidates. Animals in captivity may live longer than free-living animals and may be prone to developing progressive organ failure similar to domestic species.

MONITORING

An anesthetic plan is developed based on available history, knowledge of the species, and any available laboratory data. Monitoring physiological variables (especially cardiopulmonary) should be begun as soon as possible after induction and throughout the procedure. Most commonly used monitors can be adapted for use in the otariid (see Chapter 6). Variables that are commonly measured include heart and respiratory rates, capillary perfusion, response to painful stimuli, body temperature, hemoglobin saturation (relative SpO_2), endtidal carbon dioxide (ETCO_2), blood pressure, and blood gas levels. For otariids, the trends in the measured variables are more important than the point measurements.

Heart rate is one of the most important variables to monitor. It is determined by either palpation or observation of thoracic wall movement over the heart, just caudal to the axilla. Chest auscultation can be used, but thoracic noise is muffled compared to terrestrial mammals. Heart rate can also be determined using electrocardiogram (ECG) leads placed externally (Heard and Beusse, 1993) or attached within an esophageal probe (Haulena and Heath, 2001). Pulse oximeters also generate a pulse wave that can be used to calculate heart rate. However, the pulse wave does not reflect adequacy of tissue perfusion (see Chapter 6). The pulse oximeter probes can be clipped to the tongue (Heard and Beusse, 1993; Heath et al., 1996, 1997; Haulena et al., 2000), but the clips tend to slip off the short, thick tongue. Probes are placed on the nasal septum of larger animals. Reflectance probes can be placed rectally, vaginally, or along the buccal or gingival mucosa (Heath et al., 1996). Sudden or progressive bradycardia may be an early indication of initiation of the dive reflex. Some drugs, particularly the α_2 -agonists, also cause bradycardia.

Respiratory rate is measured by observing thoracic movement, opening of the nares, or chest auscultation. Capnography and respiratory monitors can be used to electronically calculate respiratory rate. Apnea is common in anesthetized otariids (Sedgwick, 1999) and may result from excessive anesthetic, the immobilizing drug used, or the dive reflex.

Anesthetic depth is assessed using response to various stimuli such as noise and deep pain (interdigital web pinch, ear pinch, or surgical stimulation), presence or absence of the palpebral and pupillary reflexes,

Table 41.1. Blood gas variables from the caudal gluteal vein in ten physically restrained California sea lions (*Zalophus californianus*).

Variable	Mean ± SD	Range
Na	149 ± 3	146-152
K	4.3 ± 0.5	3.6-5.3
TCO ₂	23 ± 5	17-29
iCa (mmol/L)	1.20 ± 0.07	1.07-1.31
Hct (%)	45 ± 5	37-51
Hb (g/dl)	16 ± 2	13-17
рН	7.31 ± 0.05	7.22-7.38
PCO ₂ (mmHg)	43.9 ± 4.9	38.4-53.8
PO ₂ (mmHg)	74 ± 21	45-103
HCO ₃ (mmol/L)	22 ± 4	16-27
BE	-4 ± 5	-11-2
SO ₂ (%)	91 ± 7	77–97

respiratory rate rhythm, tidal volume, and jaw tone (Work et al., 1993; Heath et al., 1996, 1997).

Peripheral body temperature measurement does not accurately reflect core because of the thick layers of insulating blubber. Flexible temperature probes are inserted at least 10 cm into the rectum of the animal (Bester, 1988; Loughlin and Spraker, 1989; Ferreira and Bester, 1999). Alternatively, esophageal probes inserted to the level of the heart (Heath et al., 1997) may give accurate core temperature readings.

Mucosal membranes (oral, rectal, and vaginal) are used for monitoring color and capillary refill time as indicators of perfusion and oxygenation (Work et al., 1993; Heath et al., 1997). Capnometer probes are attached to the endotracheal tube via filter line (Heard and Beusse, 1993; Haulena and Gulland, 2001). Elevations or sudden decreases in ETCO₂ levels may indicate ventilation and perfusion problems.

Non-invasive, oscillometric blood pressure monitoring is performed by attaching cuffs to the proximal portion of the limbs or the base of the tail. Venous blood gas samples are collected from the caudal gluteal, interdigital, or common jugular veins. Blood gas values obtained from 10 healthy California sea lions under physical restraint (Table 41.1) indicate that arterial blood is sometimes obtained from the area of the caudal gluteal vein (Haulena et al., 2001).

SUPPORTIVE CARE

Antimuscurinics

Atropine (0.02 mg/kg IM) has been recommended 10 minutes prior to immobilization to prevent bradycardia associated with the dive reflex in anesthetized otariids (Gage, 1993; Heath et al., 1996). Atropine has also been administered after injection of sedatives to control airway and oral secretion and prevent bradycardia (Spelman, 2004). However, α_2 -agonists such as medetomidine cause bradycardia. Use of atropine with medeto-

midine is contraindicated in terrestrial mammals (Cullen, 1996).

Endotracheal Intubation

Endotracheal intubation is strongly recommended for any prolonged procedure that requires a surgical plane of anesthesia (Work et al., 1993; Sedgwick, 1999). Otariid intubation is easier than in phocids, resembling intubation of terrestrial carnivores. In general, endotracheal tubes are of similar diameter to those that would be used on terrestrial carnivores of the equivalent mass. Care is taken to ensure endotracheal tubes do not extend past the pre-thoracic bifurcation of the trachea, resulting in unilateral lung intubation (McGrath et al., 1981). The mouth is opened with soft nylon straps or rope. The head and neck are held straight and in a slightly hyperextended (opisthotonic) position. Ensure table edges or other equipment does not compress the trachea and interfere with passage of the endotracheal tube (Lynch, Tahmindjis, and Gardner, 1999). Gentle manipulation is used to prevent trauma to the larynx. Standard laryngoscopes facilitate visualization of the airway (Heard and Beusse, 1993; Haulena et al., 2000). Very large adults can be intubated by manual palpation of the epiglottis (Heath et al., 1996). Cuffed endotracheal tubes are used to prevent aspiration. It is important not to cause tracheal injury by over-inflating the cuff. Endotracheal tubes can be secured over the maxilla or mandibles using rolled gauze, rope, or tape passed caudal to the canine teeth.

Thermoregulation

Body temperature fluctuations resulting in either hypothermia or hyperthermia can occur in anesthetized otariids. It is particularly important to monitor temperature in field conditions in which control of the environment is more difficult. Temperature changes are influenced by the drugs used, the species, size, geographic location, and physiological status of the animal. For example, larger animals have a greater tendency to hyperthermia than smaller animals (Work et al., 1993). Some drugs (e.g., ketamine) may cause hyperthermia (Sepulveda, Ochua-Acuna, and McLaughlin, 1994), whereas others (e.g., isoflurane) cause vasodilation that promotes hypothermia (Loughlin and Spraker, 1989; Work et al., 1993). Profound hyperthermia was seen in a late-term pregnant California sea lion that was anesthetized using medetomidine and ketamine. Shelter from rain, wind, and sun, although maintaining adequate ventilation, is recommended to prevent temperature irregularities. A variety of commercially available heating blankets, heated surgical tables, hot water bottles, wraps, and insulating pads can be used to prevent hypothermia (Work et al., 1993; Sepulveda, Ochua-Acuna, and McLaughlin, 1994; Heath et al., 1997). Ice or cold water applied to extremities is used to treat hyperthermia.

Vascular Access

Vascular access for placement of catheters for fluid and emergency drug administration is difficult in small animals, hypothermic individuals, or otariids anesthetized with certain drugs (e.g., α_2 -agonists). Some species have readily accessible interdigital veins in the pelvic limbs. However, these are not accessible in some species (e.g., California sea lion). Other accessible veins for catheterization include the cephalic, jugular, subclavian, and vessels running along the digits of the hind flipper. An indwelling catheter was maintained by the author for 4 days in a juvenile California sea lion using the common jugular vein.

Ventilation

Low SpO_2 values (less than 85%) have been reported in sea lions immobilized with zolazepam/tiletamine (Heath et al., 1996) and medetomidine/ketamine (Haulena et al., 2000). This effect is greater in animals not intubated and provided supplemental oxygen. Conversely, sea lion pups maintained with isoflurane in oxygen maintained higher SpO_2 values (Heath et al., 1997). This may be result from the drugs used, anesthetic depth, or animal's physiology. Low SpO_2 levels indicate the anesthetist should be prepared to intubate, provide oxygen therapy, and assist ventilation.

High ETCO₂ (greater than 70 mmHg) levels (Heard and Beusse, 1993; Haulena and Gulland, 2001) associated with acidemia (pH less than 7.15) in anesthetized California sea lions support the need for assisted mechanical ventilation in some animals (Haulena, Heath, and Gulland, 2001). Some drugs are more commonly associated with hypoventilation and hypercapnia. Animals anesthetized for prolonged periods, maintained at deep anesthetic planes and positioned in a manner that interferes with normal thoracic expansion, are particularly prone to developing hypercapnia. Conversely, hyperventilation of California sea lions has resulted in alkalemia (pH greater than 7.5).

In anesthetized otariids, mechanical ventilation is recommended at a starting tidal volume of 15 ml/kg and a rate of 8 to 10 breaths per minute (Haulena, Heath, and Gulland, 2001). Capnometry is essential with mechanically assisted ventilation to adjust tidal volume and rate to maintain normocapnia.

SEDATION

The use of a variety of IM sedative drugs may facilitate physical or mechanical restraint and aid induction with other drugs (e.g., isoflurane) (Gales, 1989). Oral diazepam (0.1–0.2 mg/kg) used prior to transport aids physical restraint of some animals. More reliable sedation is achieved with midazolam in California sea lions (0.15–0.2 mg/kg IM) and fur seals (0.25–0.35 mg/kg IM) (Lynch, Tahmindjis, and Gardner, 1999). Benzodiazepines can be reversed with flumazenil

(Karesh et al., 1997). Butorphanol (0.05–0.2 mg/kg IM) has been used for mild sedation and analgesia. Combination of midazolam and butorphanol results in an increased level of sedation. Medetomidine (70 μ g/kg IM) is recommended for sedation of sea lions for electroencephalography because of its apparent lack of interference with brain wave patterns (Dennison et al., 2005). Although sedation was variable, placement of multiple percutaneous leads for recordings was accomplished for more than 30 minutes.

CHEMICAL IMMOBILIZATION

Drugs commonly used to immobilize otariids are discussed in the following section. Table 41.2 summarizes drug dosages from recent studies. Several reviews have been written and should be referred to for a complete list of pinniped immobilization methods (Gales, 1989; Williams, Williams, and Stoskopf, 1990; Lynch, Tahmindjis, and Gardner, 1999; Haulena and Heath, 2001).

Zolazepam/Tiletamine

The advantages of this combination include small injection volume, low cost, and dependable deep sedation and immobilization. However, some studies report significant mortality, prolonged recovery, and a narrow margin of safety (Heath et al., 1996; Dabin, Beauplet, and Guinet, 2002). Zolazepam/tiletamine (1.7 mg/kg IM) in California sea lions is administered 10 minutes after atropine (0.02 mg/kg IM) (Gage, 1993). A slightly lower dosage (0.9-1.3 mg/kg IM) is recommended in subantarctic fur seals (Arctocephalus tropicalis). Additional "top-up" doses to increase anesthetic depth have been associated with increased mortality (Heath et al., 1996). However, additional ketamine has been used successfully without mortality (Karesh et al., 1997). The combination is partially reversed with flumazenil (Karesh et al., 1997).

Medetomidine/Ketamine

In California sea lions, the combination of medetomidine (140 μ g/kg IM) and ketamine (2.5 mg/kg IM) provides effective and safe immobilization that is reversed by atipamezole (0.2 mg/kg IM). Animals were premedicated with atropine (0.02 mg/kg IM). Disadvantages of this combination in sea lions include moderately variable anesthetic depth, large injection volume when commercially available products are used, and high cost (Haulena et al., 2000).

Medetomidine/Zolazepam/Tiletamine

The combination of medetomidine ($70 \mu g/kg IM$) and zolazepam/tiletamine (1 mg/kg IM) produced reversible (atipamezole 0.2 mg/kg IM), reliable anesthesia (Haulena and Gulland, 2001). Injection volume and cost were much less than for medetomidine/ketamine.

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Species	Ν	Drug(s)	Dosage	Route	Mortality	Comments	Reference
Arctocephalus australis South American fur seal	32	Tiletamine/Zolazepam	1.43 mg/kg	IM dart	%0	Partial reversal with flumazenil	Karesh et al., 1997
Arctocephalus australis South American fur seal	4	Tiletamine/Zolazepam, Ketamine	1.43 mg/kg 0.81 mg/kg	IM dart IM	%0	Supplemental ketamine given owing to insufficient sedation; partial reversal with flumazenil	Karesh et al., 1997
Arctocephalus australis South American fur seal	∞	Tiletamine/Zolazepam, Ketamine	1.15 mg/kg 0.27 mg/kg	IM dart	%0	All administered together; partial reversal with flumazenil	Karesh et al., 1997
Arctocephalus australis South American fur seal	1	Ketamine/Midazolam	$1\mathrm{mg/kg}$ $0.1\mathrm{mg/kg}$	IM dart	%0		Karesh et al., 1997
Arctocephalus forsteri New Zealand fur seal	2	Isoflurane	1.2%-4.0%	Ш	%0		Gales and Mattlin, 1998
Arctocephalus gazella Antarctic fur seal	172	Tiletamine/Zolazepam	1.2-1.7 mg/kg	IM dart	3%	Respiratory depression	Boyd et al., 1990
Arctocephalus gazella Antarctic fur seal	30	Ketamine	$6.9\pm0.1\mathrm{mg/kg}$	IM dart	%0	Muscle tremors	Boyd et al., 1990
Arctocephalus gazella Antarctic fur seal	23	Ketamine/Diazepam		IM dart IM dart	4%		Boyd et al., 1990
Arctocephalus gazella Antarctic fur seal	45	Ketamine/Xylazine	$7.3 \pm 0.3 \mathrm{mg/kg}$ $0.6 \pm 0.02 \mathrm{mg/kg}$	IM dart IM dart	7%		Boyd et al., 1990
Arctocephalus gazella Antarctic fur seal	14	Ketamine/Xylazine	3.8–10.8 mg/kg 0.7–2.0 mg/kg	M M	14%	Poor sedation with Ketamine $\leq 5.6 \text{ mg/kg}$	Bester, 1988
Arctocephalus gazella Antarctic fur seal	7	Ketamine/Xylazine	5.6-7.8 mg/kg 0.5-1.3 mg/kg	IM dart	%0		Ferreira and Bester, 1999
Arctocephalus phillipi Juan Fernández fur seal	12	Ketamine/Diazepam	2.16–6.76 mg/kg 0.04–0.28 mg/kg	M	17%	Decreased induction and recovery times than when used IV; variable plane of anesthesia	Sepulveda et al., 1994
Arctocephalus phillipi Juan Fernández fur seal	10	Ketamine/Diazepam	2.16–6.76 mg/kg 0.04–0.28 mg/kg	IV	%0	Deeper immobilization compared with IM	Sepulveda et al., 1994
Arctocephalus pusillus pusillus South African fur seal	27	Ketamine	4.3-7.8 mg/kg	IM dart	19%	Variable anesthesia	David et al., 1988
Arctocephalus pusillus pusillus South African fur seal	7	Ketamine/Xylazine	4.2–5.2 mg/kg 0.6–0.9 mg/kg	IM dart IM dart	29%	Xylazine dosage estimated	David et al., 1988
Arctocephalus pusillus pusillus South African fur seal	5	Carfentanil/Xylazine	6–18 µg/kg NA	IM dart IM dart	NA	20% of animals given combination with carfentanil died; apnea, muscle convulsions, variable plane of anesthesia	David et al., 1988

Arctocephalus pusillus South African fur seal	_	Carfentanil/Xylazine/ Azaperone/	6–18 µg/kg NA NA	IM dart IM dart IM dart	na	20% of animals given combination with carfentanil died; apnea, muscle convulsions, variable plane of anesthesia	David et al., 1988
Arctocephalus pusillus pusillus South African fur seal	7	Carfentanil/Xylazine/ Azaperone/Ketamine	6–18 µg/kg NA NA NA	IM dart IM dart IM dart IM dart	na	20% of animals given combination with carfentanil died; apnea, muscle convulsions, variable plane of anesthesia	David et al., 1988
Arctocephalus pusillus pusillus South African fur seal	2	Carfentanil/Xylazine/ Ketamine	6–18 µg/kg NA NA	IM dart IM dart IM dart	na	20% of animals given combination with carfentanil died; apnea, muscle convulsions, variable plane of anesthesia	David et al., 1988
Arctocephalus pusillus pusillus South African fur seal	15	Xylazine/Zzaperone	0.57-2.0 mg/kg 0.57-2.0 mg/kg	IM dart IM dart	7%	Sufficient for branding, short immobilization time	David et al., 1988
Arctocephalus pusillus pusillus South African fur seal	2	Droperidol	NA	IM	20%		David et al., 1988
Arctocephalus tropicalis Subantarctic fur seal	58	Ketamine	1.9-2.8 mg/kg	IM	%0	Sufficient for tooth extraction, some tremors noted	Dabin et al., 2002
Arctocephalus tropicalis Subantarctic fur seal	32	Ketamine/Xylazine	3.1–11.4 mg/kg 0.3–1.7 mg/kg	IM dart	13%	Variable anesthesia	Ferreira and Bester, 1999
Arctocephalus tropicalis Subantarctic fur seal	49	Tiletamine/Zolazepam	0.7-1.9 mg/kg	IM	4%	Prolonged recovery; apnea requiring artificial respiration	Dabin et al., 2002
Eumetopias jubatus Steller's sea lion	29	Tiletamine/Zolazepam	1.8–8.1 mg/kg	IM dart	21%	Best results; 1.8–2.5 mg/kg	Loughlin and Spraker, 1989
Eumetopias jubatus Steller's (northern) sea lion	51	Tiletamine/Zolazepam, Isoflurane	1.6-3.3 mg/kg	IM dart IM dart IH	10%		Heath et al., 1996
<i>Otaria byronia</i> South American sea lion	13	Tiletamine/Zolazepam	2.75 mg/kg	M	%0	Flumazenil 1 mg for every 20-25 mg of tiletamine and zolazepam for reversal	Karesh et al., 1997
<i>Otaria byronia</i> South American sea lion	7	Isoflurane	NA	IH	%0		Karesh et al., 1997
Phocarctos hookeri Hooker's (New Zealand) sea lion	29	Isoflurane	0.8%-4.0%	IH	%0		Gales and Mattlin, 1998
Zalophus californianus California sea lions	4	Detomidine/Ketamine, Isoflurane	40–55 µg/kg 2.0–4.3 mg/kg 1%–5% in oxygen	M M H	%0		Heard and Beusse, 1993
Zalophus californianus California sea lions	09	Tiletamine/Zolazepam	1.7 mg/kg	IM	%0	Apnea	Gage, 1993
Zalophus californianus California sea lion	115	Isoflurane	0.75%-3%	IH	%0		Heath et al., 1997
Zalophus californianus California sea lion	30	Halothane	0.75%-5%	IH	3%		Work et al., 1993

Species	N	Drug(s)	Dosage	Route	Mortality	Comments	Reference
Zalophus californianus California sea lion	35	Medetomidine/Ketamine	140 µg/kg 2.5 mg/kg	M M	%0	Variable anesthesia; reversal with atipamezole	Haulena et al., 2000
Zalophus californianus California sea lion	16	Medetomidine/Ketamine, Isoflurane	140 µg/kg 2.5 mg/kg 1%-5%	M M H	%0	Reversal with atipamezole	Haulena et al., 2000
Zalophus californianus California sea lion	17	Medetomidine, Tiletamine/Zolazepam	70 µg/kg 1 mg/kg	M M	%9	Reliable anesthesia; reversal with atipamezole; ataxia and disorientation during recovery in some animals	Haulena and Gulland, 2001
Zalophus californianus California sea lion	22	Medetomidine, Tiletamine/Zolazepam, Isoflurane	70 µg/kg 1 mg/kg 1%-5%	M H	%0	Reliable anesthesia; reversal with atipamezole; ataxia and disorientation during recovery in some animals	Haulena and Gulland, 2001
Zalophus californianus California sea lion	7	Medetomidine/ Midazolam/Butorphanol/ Isoflurane	10–13 µg/kg 0.2–0.26 mg/kg 0.2–0.4 mg/kg 0.5%–2.0%	HERE	%0	Two animals anesthetized 13 times; Reversal with atipamezole, flumazenil, naltrexone	Spelman, 2004

Table 41.2.(Continued)

Adverse effects observed during recovery included tremors, ataxia, and disorientation. These were less than with zolazepam/tiletamine alone, but occur more often than with medetomidine/ketamine. Animals were premedicated with atropine (0.02 mg/kg IM). One mortality did occur in the study. Consequently, a lower medetomidine dosage (40 μ g/kg) in combination with zolazepam/tiletamine is recommended.

Medetomidine/Butorphanol/Midazolam

A combination of medetomidine (10–13 µg/kg), midazolam (0.2–0.26 mg/kg), and butorphanol (0.2–0.4 mg/kg) IM was evaluated in California sea lions (Spelman, 2004). The combination is completely reversible using atipamezole (0.05–0.06 mg/kg IM), flumazenil (0.0002–0.002 mg/kg IM), and naltrexone (0.1 mg/kg IM), respectively. The combination produced safe, light anesthesia in animals that was supplemented with isoflurane for deeper planes of anesthesia. Atropine (0.02 mg/kg IM) was given after injection of the combination.

Inhalant Anesthetics

Inhalant anesthetics, including isoflurane (Heard and Beusse, 1993; Heath et al., 1996, 1997; Gales and Mattlin, 1998; Haulena et al., 2000), sevoflurane, and halothane (Work et al., 1993) have all been used in otariids. The safest anesthesia with the best recovery characteristics has been obtained with isoflurane and sevoflurane. Otariids uptake anesthetic gases very rapidly and efficiently and are readily induced with a mask. Controlled studies on the efficacy of mask induction and maintenance of anesthesia with an inhalant are few for marine mammals. However, California sea lions, New Zealand fur seal (Arctocephalus forsteri) bulls, and adult female New Zealand sea lions (Phocarctos hookeri) appear to be more rapidly masked to anesthetic depths in comparison with terrestrial species (Heath et al., 1997; Gales and Mattlin, 1998). The use of inhalant anesthetic agents alone appears to be a reliable and safe method of anesthesia in otariids if it is possible to accomplish restraint and masking (Figure 41.1). Premedication and induction with intramuscular drugs facilitates masking and maintenance of anesthesia with an inhalant agent if the animals cannot be masked voluntarily or with physical restraint (Heard and Beusse, 1993; Heath et al., 1996; Haulena et al., 2000; Haulena and Gulland, 2001). Once anesthesia has been attained reversible induction agents may be antagonized.

ANALGESIA

There are very few studies evaluating the use of analgesics in otariids. Use and dosage of analgesic agents has been based on extrapolation from other species and personal experience. Analgesics that have been used with good clinical response in otariids include opiates,



Figure 41.1. Training a Steller sea lion (Eumetopias jubatus) for voluntary acceptance of a mask for induction with isoflurane at the Vancouver Aquarium. (Photo courtesy of the University of British Columbia Marine Mammal Research Unit.)

non-steroidal anti-inflammatory drugs (NSAIDs), and α_2 -agonists. The most commonly used opioid is butorphanol (0.05–0.2 mg/kg PO, IM, or IV q6 hours). NSAIDs used by the author include flunixin meglumine (1 mg/kg IM q24 hours) for up to 3 days, ketoprofen (1 mg/kg IM q24 hours) for up to 5 days, buffered acetylsalicylic acid (5 mg/kg PO q 24 hours) for up to 5 days, and carprofen (2–4 mg/kg PO q 24 hours) for up to 14 days (Dold, Haulena, and Gulland, 2004). For additional analgesia, butorphanol has been combined with an NSAID. Medetomidine (10–40 µg/kg) has also been used to provide analgesia.

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Walrus David B. Brunson

INTRODUCTION

Marine mammals have the reputation of being difficult to chemically immobilize or anesthetize. Of this group of animals walruses may rank as one of the most difficult. The large size, limited vascular access, and propensity for sudden physiological changes during restraint have led to their reputation of high anesthetic risk. High mortality rates have been reported with both opioids and dissociative anesthetics but are most likely owing to severe respiratory and circulatory compromise when the animals are anesthetized out of the water. Respiratory arrest is commonly reported during immobilization with potent opioids. Despite ventilatory support these large animals develop circulatory failure.

There are two subspecies of Walruses; the Atlantic walrus, *Odobenus rosmarus rosmarus*, and the Pacific walrus, *Odobenus rosmarus divergens*. A third subspecies has been proposed, the Laptev Sea walrus, *Odobenus rosmarus laptevi*, but this is not commonly recognized as such.

The walrus is a large and powerful pinniped. The skin is typically a cinnamon-brown color that is covered by short coarse hair. As the animal ages the skin becomes lighter. Walruses have enlarged upper canine teeth commonly referred to as tusks. In the Atlantic subspecies, the males measure 300 cm and weigh 1,200 kg. Females measure 250 cm and weigh 750 kg. At birth pups are 140 cm long and weigh 50 kg. The Pacific walrus is slightly larger with males being up to 360 cm long and weighing up to 1600 kg. Pacific walrus females are 260 cm long and weigh approximately 1250 kg. Young Pacific walrus pups measure 140 cm and weigh 60 kgs (Garlich-Miller and Stewart, 1999).

ANATOMY AND PHYSIOLOGY RELATED TO ANESTHESIA

The physiological adaptations of the walrus for extended swimming and deep diving present challenges that are unique to aquatic mammals. Because walruses can submerge for extended time periods for foraging at the sea bottom, they are capable of prolonged breath holding. Additionally, the simultaneous occurrence of low heart rates with breath holding has close similarities to the classic "dive reflex." However, unlike the normal diving physiology, apnea and bradycardia during chemical immobilization are associated with high mortality. Normal dive responses are not associated with lasting metabolic derangements or cardiac failure. It appears that during chemical immobilization or general anesthesia the physiological dive mechanisms do not function normally. A necropsy finding of a captive walrus showed disseminated myocardial fibrosis and atherosclerosis, which was attributed as the cause of death. Underlying myocardial disease would increase the risk of anesthesia (Gruber, Peters, and Knieriem, 2002).

The upper airway of walruses is characterized by small nostrils with large muscles to close the openings during submersion. The nasal passages are small and the nasal turbinates are such that there is no large meatus. This adaptation prevents water from passing through the nose into the pharynx and trachea. The oral cavity is large and characterized by a high arched hard palate. The walruses tongue is large and thick. Because the tongue lacks thin edges standard veterinary pulse oximetry probes are not easily placed on the tongue. The lower jaw moves between the large upper canine teeth (tusks). Even in very large individuals the rostral opening to the mouth is no more than 10 to 12 cm in width and height. Because of the limited size of the opening, smaller walruses are difficult to manually direct an endotracheal tube into the larynx as is done in cattle.

Walruses have a unique pharyngeal pouch that can be inflated to provide bouncing while resting on the ocean surface. Although this adaptation seems to be more highly developed in wild free-ranging walruses it may also present a potential problem for airway management in captive raised walruses (Fay, 1969). During tracheal intubation it is important to direct the tube through the larynx and not into the pharyngeal pouch.

Because of the large size and physical power of walruses most procedures have to be performed under the effects of immobilizing drugs or general anesthetics. Local anesthetic can be used to provide analgesia for surgical procedures. The thick skin and heavy layer of insulating fat present mechanical challenges for effective regional nerve blocks. However, infiltration of the skin can be performed to provide effective local anesthesia. Both lidocaine HCl and bupivacaine HCl are effective for blocking pain.

Opioid analgesics have been used for capture and immobilization in walruses (DeMaster et al., 1981; Gales, 1989; Griffiths et al., 1993; Lynch, Tahmindjis, and Gardner, 1999). As with other marine mammals analgesia in addition to immobilization is assumed. Of the opioid analgesics, meperidine and butorphanol have been used with benzodiazepines or α_2 -agonists. Assessment of the analgesic effects of opioids has been limited to the responses observed during immobilization.

Physical restraint of untrained wild adult walruses is impractical. Captive walruses can be conditioned to enable physical examination, including oral examination and thoracic auscultation. Cargo nets can be used for young animals but have limited effectiveness in animals greater than 100 to 150 kg of body weight.

Vascular Access

The heavy subcutaneous fat layer and the thickness of walrus skin prevent identification and access to veins in the cervical region or the appendages. Venous access can be obtained through the dorsal extradural intravertebral vein (EIV) and the gluteal vein. Placement of a catheter into the dorsal extradural intravertebral vein has been described (Stetter et al., 1997). The epidural IV access can be used for fluid administration, emergency drugs, and intravenous anesthetic administration.

Since intravenous access is difficult through peripheral veins, vascular access can be obtained via the epidural venous sinus. Needle placement is identical to placement of epidural needles or catheters via the lumbosacral space. To locate the site for access to the EIV, palpate the wings of the ileum on each side of the spinal column. These bony prominences can be found even in animals with normal body fat and in healthy condition. A Tuohy needle is recommended to assist in directing the catheter cranially into the vein. The needle is placed on the midline approximately 3 to 5 cm behind a line transecting the midline from the cranial aspects of each ileum. This should be approximately at the third to fourth lumbar vertebra (L3-L4). The landmarks for the proper access site are the same as those used for epidural anesthesia in the dog or cat. In adult walruses a 16- or 17-gauge 8.9-cm-long needle is necessary to access the EIV. Advance the needle into the animal at a perpendicular angle to the skin. A syringe can be placed on the needle and gentle aspiration used to determine entrance into the vein.

Vascular access from the flippers has been described in phocid seals but not walruses. Attempts to obtain blood samples following the landmarks described for seals are as follows. At the level of the proximal edge of the interdigital webbing of the second and third digits, insert a 37-mm (1.5-inch) 19-gauge needle at a 10- to 20-degree angle until the blood is aspirated into the syringe. Blood obtained will most often be of mixed arterial and venous origin (Geraci, 1981).

An alternative vascular access location is the caudal gluteal vein. A needle is inserted lateral to the sacral vertebra approximately one-third of the distance from the femoral trochanter to the base of the tail. In adult walruses a 12.5-cm-long needle is necessary to reach the vessel. The needle should be held perpendicular to the skin and advanced slowly until blood can be aspirated into a syringe.

Injection Sites

The walrus, like seals and sea lions, have relatively small pelvic limbs. The pelvis, femur, and tibia are short and the associated muscles are small in relation to the size of the animal. The femur of an adult 1,500-kg pacific walrus is approximately 12 to 14 inches in length. In addition the upper pelvic limb is not well demarcated, resulting in injections often occurring at or below the knee joint. The muscles of the hind limbs and pelvis can be used for IM injections but are relatively smaller than the epaxial muscles.

The best sites for intramuscular injections are the large muscles of the back. The epaxial muscles are large and well developed. The areas caudal to the last rib and cranial to the pelvis on both sides of the vertebral column provide a large target area for remote drug injection. The muscles of the front limbs can also be used for IM drug administration. Caution should be used to ensure that injections do not occur into the large cervical blood vessels, which are located cranial to the front legs.

During immobilization and anesthesia injections can be made into the base of the tongue. Sublingual injections have the advantage of rapid absorption owing to the high blood flow to the tissue. In emergencies, sublingual injections provide a readily available route for cardiac and respiratory support drugs. Alternatively, emergency drugs can be administered by flushing the drugs into the lungs via the endotracheal tube. A long semi-rigid piece of plastic tubing can be passed through the ET tube and the medications flushed into the airway. Dilution of the drugs or flushing the tubing with sterile water is recommended to ensure that the entire drug dosage has been administered. Antagonists for immobilization drugs may also be given by these routes when the end of the immobilization has been reached.

Endotracheal Intubation

Intubation of walruses is relatively easy to perform. Key to intubation includes extension of the neck to straighten the oral-laryngeal axis. This is facilitated by positioning the walrus in sternal recumbency. If the animal has large tusks, they can be used to prop up the head and extend the neck. Small ropes or towels can be used to aid positioning for intubation. Because of the highly arched hard palate, using a separate rope or towel around each tusk allows better access to the oral cavity than a single one rope passed across the oral cavity. Palpation of the larynx and manual directing the endotracheal tube into the trachea is recommended if possible. Because of the small size of the oral cavity of even large walruses it may be difficult to pass a large endotracheal tube while palpating the larynx. In these cases the use of a small-diameter stylet is recommended. The stylet must be at least twice as long as the endotracheal tube. Palpate the larynx as described above and pass the stylet through the larynx and into the trachea. The endotracheal tube is then fed over the stylet and into the trachea. Blind intubation is not recommended because of the difficulty in correct placement and the potential for the ET tube to enter the esophagus or pharyngeal pouch.

Tracheal intubation is facilitated by muscle relaxation during immobilization and anesthetic induction. Opioids and dissociatives immobilization techniques are frequently associated with extensive muscle rigidity. Small dosages of Propofol (40–60 mg) via the EIV have been used to produce muscle relaxation and facilitate endotracheal intubation.

SEDATIVE AND ANESTHETIC TECHNIQUES

Sedation and Analgesia of Captive Walruses

Captive walruses are usually immobilized with a combination of midazolam (0.1 mg/kg) and meperidine (2.2 mg/kg) (Klein et al., 2002). Atropine (0.04 mg/kg) is also recommended to prevent vagally induced bradycardia. Intramuscular injections into the hip or epaxial muscles are the recommended injections sites. A long needle (3–4 in.) is necessary to ensure effective drug absorption.

Heart rate during the onset of immobilization and anesthesia is usually between 80 and 100 beats per minute (bpm). As anesthesia deepens the heart rate slows to around 60 bpm. Apnea is a common sequel to anesthetic or immobilization drugs. Ventilatory support is essential when working with these animals. End tidal gas monitoring is recommended to assess the efficacy of ventilation and determine the relative anesthetic concentrations in the animal. Spontaneous ventilation is likely to be inadequate and methods for assisting ventilation should be available. In contrast to the awake animal's ability to breath-hold for long time periods, apnea during immobilization and anesthesia is

associated with respiratory and metabolic acidosis, arrhythmias, and poor anesthetic delivery. For this reason controlled ventilation coupled with expired gas monitoring is important for immobilization or anesthesia.

Specific analgesic techniques have not been studied in walruses. Analgesic methods used in other marine mammals should be considered to decrease stress associated with painful procedures or conditions. As previously discussed, local anesthetics are effective if injected around the surgical site or on sensory nerves to a region. As with other species total local anesthetic dosages should be kept below 2 mg/kg to avoid potential local anesthetic toxicity. Opioid analgesics used as a part of chemical immobilization techniques are believed to provide reduction in pain perception, modulation, and transduction. Chronic pain management has not been addressed in walruses and no recommendations can be made for the use of anti-inflammatory drugs at this time.

Immobilization Techniques

Whether immobilizing a walrus in captivity or in the wild, the attendant problems are similar. The drugs must be administered via intramuscular injection and from a distance. For this reason drug volumes must be small and choices are restricted to α_2 -agonists, benzodiazepines, opioids, and dissociative class of drugs. These drug groups have been used successfully; however, mortalities have also been associated with all drug groups. The reversibility of α_2 -agonists, benzodiazepines, and opioids has made them the preferred drugs for some situations.

Based on early studies in marine mammals, meperidine was shown to be an effective sedative and immobilization drug in a variety of species (Josephs and Cornell, 1988). Meperidine was administered by hand injection to 10 walruses at a dosage of 0.23 and 0.45 mg/kg. Sedation and restraint were moderate without apparent detrimental effects. If used as an analgesic, meperidine is associated with obvious sedation (Cornell, 1978). As a result of clinical experience, a higher dose of meperidine (2.2 mg/kg) is frequently used to immobilize captive walruses when combined with midazolam (0.1 mg/kg). It is recommended, because of the high incidence of bradycardia during sedation, that atropine (0.04 mg/kg) intramuscularly (IM), subcutaneously (SQ), or intravenously (IV) be included in the immobilization technique (Klein et al., 2002). A long needle (3-4 in.) is necessary to ensure effective drug absorption.

If needed, the author has used small boluses of propofol (40–60 mg) via the EIV sinus to provide unconsciousness and muscle relaxation, and facilitate endotracheal intubation. The use of propofol decreased the need for higher doses of the immobilization drugs, and the associated muscle relaxation appears to facilitate

spontaneous ventilation. Similarly, ultra–short-acting barbiturates (e.g., thiamylal sodium) have been used successfully to produce general anesthesia in walruses: 3.3 to 4.8 mg/kg with one-half of the calculated dose administered initially and the additional drug given to effect as needed (Walsh et al., 1990).

Isoflurane has been used to maintain general anesthesia in walruses. However, because of the low blood:gas solubility of sevoflurane, both uptake and elimination are faster and may improve the ability to reach surgical anesthesia and have shorter recovery times than with isoflurane. Since the cardiovascular and respiratory depressive effects of isoflurane and sevoflurane are similar, the lower solubility of sevoflurane is of significant advantage in walruses. Oxygen flow rates and vaporizer settings are similar to equine anesthesia. Oxygen should be set at greater than 4 L/minute to ensure delivery of anesthetic and oxygen for metabolic needs. Initial vaporizer settings likely should be between 3.0% and 4.5%; however, vaporizer settings should be reduced in anticipation of equilibration of the animal with the anesthetic machine. Maintenance levels of 2.0% to 2.5% isoflurane and 2.5% to 3.0% sevoflurane are expected.

The use of highly potent opioid analgesics for immobilization of walruses has proved to be less than ideal. Complications include apnea, muscle spasms, rigidity, and death. Adult male Atlantic walruses on a land haul out were effectively immobilized with carfentanil with an intramuscular dose of 2.7 to 3.0 mg. Muscle spasms were associated with the onset of immobilization. All of the animals had extended periods of apnea; tracheal intubation was not possible because of muscle rigidity (Lanthier, Stewart, and Born, 1999; Lanthier and Stewart, 2002). The estimated effective dosage range was 4 to 5 µg/kg.

Many factors make accurate drug dosing difficult in field situations. The body weight can only be estimated prior to drug administration dart placement and vascularity of the injection site all affect the ultimate success of remote drug delivery. Pacific walruses injected with similar carfentanil dosages were not adequately immobilized despite the presence of apnea and muscle spasms.

A field study was performed to test combinations of medetomidine with carfentanil in adult Pacific Walruses. Medetomidine was selected because of the presence of an effective antagonist (atipamezole) and availability of a concentrated formulation that minimized dart size and injection volume. The addition of medetomidine with carfentanil would likely decrease the opioid dose and improve muscle relaxation (Mulcahy et al., 2003). A medetomidine dose of 30 mg was combined with carfentanil doses that varied from 0.06 to 3.0 mg per animal. At the 0.06 mg carfentanil dose, immobilization was inadequate; at the 3.0 mg dose, severe respiratory and circulatory depression occurred that was judged to be life

threatening. Carfentanil doses of 0.15 and 0.3 mg with 30 mg of medetomidine enabled approach and handling, but apnea occurred and immediate reversal of both drugs was administered. Because of the low numbers of animals, it was not possible to further evaluate this combination. It should be noted that the addition of medetomidine markedly decreased the carfentanil needed for immobilization, although respiratory depression was still severe.

Field immobilizations with etorphine HCl have had similar effects. Dosages between 4.0 and 15.5 mg/adult male based on estimated body weight were used in field immobilizations of Pacific Walruses, with or without reversal with either diprenorphine or naloxone. A dose of 7 mg/adult male was used for the standard dose. Overall mortality rates varied but were in the range of 15% to 20% (Hill 1992; Griffiths et al., 1993).

Because of the rapid onset of severe respiratory depression associated with potent opioid administration in walruses, opioid antagonists should be available. Naltrexone is recommended because the antagonism lasts beyond the expected effects of opioid agonist. A naltrexone dose of 0.1 mg/kg of the estimated body weight has been used in field immobilization situations with complete reversal occurring in less than 5 minutes. If the immobilization technique includes the use of an α_2 -agonist such as medetomidine atipamezole should be administered if full immediate recovery is desired. A 5:1 ratio of atipamezole to medetomidine is recommended for complete reversal.

Tiletamine and ketamine have been used to immobilize free-ranging walruses. The principal problem associated with dissociative chemical restraint is the long duration of effect and the lack of a reversal agent. Because walruses are often immobilized near water, it is imperative that conditions prevent the partially anesthetized animal from entering water.

Tiletamine and zolazepam (telazol or zolatil) at a dose of 1.4 to 2.2 mg/kg IM have been studied for chemical restraint of walruses. Induction time ranged from 14 to 29 minutes and the duration of immobilization lasted from as short as 75 minutes to as long as 220 minutes. The induction and recoveries were reported to be smooth. Apnea was not reported, although one of the three animals died during recovery (Griffiths et al., 1993).

Atlantic walruses have also been immobilized with a combination of telazol and medetomidine. A total dose of telazol and 100 mg of medetomidine (approximately 3.3 mg /kg telazol and 17 μ g/kg medetomidine) were administered by dart to two animals. The respiration rate varied between 10 and 12 per minute throughout the procedure. Despite oxygen supplementation via a nasal cannula, pulse oximetry showed relatively low oxygen concentration (37%–79%) (Lanthier and Stewart, 2002). Atipamezole was used to antagonize medetomidine. Three additional walruses (one male and two

females) were injected with a total dose of 2 gm of ketamine and 90 mg of medetomidine (approximately 2.5–4.0 mg/kg ketamine and 11–18 μ g/kg medetomidine). In each case, the respiration rate appeared to be normal (rate and depth). Immobilization occurred in 15 minutes. None of the walruses showed muscle spasms. Procedure length varied between 16 and 40 minutes. Atipamezole was injected intravenously and intramuscularly 50/50 as the antagonist (approximately 9.5–19 μ g/kg). Recoveries were smooth and rapid (6–23 minutes) (Lanthier and Stewart, 2002).

Monitoring and Supportive Care

Baseline heart rate and respiratory rates should be taken prior to drug administration. Changes associated with the onset of the effects of immobilization drug can be used to determine the time to approach and intervene. Because apnea is often associated with anesthesia of all marine mammals and especially walruses, ventilation rate is essential to monitor during all phases of handling. Adequacy of ventilation is best determined by measurement of end-tidal carbon dioxide (ETCO₂) or blood gas measurements. CO₂ can be monitored with battery operated side-stream style monitors with a catheter placed into the animal's airway or from an endotracheal tube in the animal is intubated. Blood gases can be measured on blood samples taken from any vessel, including the IVS.

Heart rate can be determined by observation of movement of the animal's chest wall. Once at the animal's side, auscultation of the heart with a stethoscope or use of an electrocardiograph (ECG) to determine the rate and rhythm of the heart is essential to detect early changes in cardiac function. The use of a pulse oximeter has proved difficult because of the lack of places to position the sensing probes. The author has found that a reflectance style pulse oximeter probe placed against the oral mucosa or rectum has worked intermittently.

SUMMARY

Chemical restraint, sedation, analgesia, and anesthesia of walruses are some of the most challenging medical procedures facing a wildlife biologist or veterinarian. The large size of the animal coupled with thick skin, insulating fat, inaccessible veins, and propensity for adverse responses to all central nervous system depressants result in a high mortality rate associated with these procedures. In addition the environment in which these animals live presents major strategic challenges to chemical immobilization and anesthesia. Even in captivity the proximity to water creates an additional complexity to medical intervention.

Opioids and benzodiazepine drugs have proved to be effective for chemical restraint and anesthesia induction. The availability of antagonists provides an option for blocking the depressant effects of these drugs when the

procedure is completed or in the case of complications. Walrus anesthesia should be performed only with extensive planning and preparation for the almost certain occurrence of respiratory depression. The ability to intubate and ventilate the immobilized walrus is essential. In addition to reversal drugs, respiratory stimulants and cardiovascular support drugs should be available.

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Cetaceans

Chris Dold and Sam Ridgway

TAXONOMY AND BIOLOGY

Cetaceans (whales, dolphins, porpoises) are mammals whose ancestors developed on land. Around 55 million years ago these ancestors went back to the water (Gingerich et al., 1983), evolving anatomically, physiologically, and behaviorally for a completely aquatic existence. Most clinical experience has been with the bottlenose dolphin (Tursiops truncatus, T.t. gilli, T.t. aduncus), the species most commonly found in display, research and rehabilitation facilities. Other odontocete species, including the killer whale (Orcinus orca), the beluga or white whale (Delphinapterus leucas), the pacific white-sided dolphin (Lagenorhynchus obliquidens), and the false killer whale (Pseudorca crassidens) have been successfully managed in zoos and aquaria for many years. A growing amount of clinical experience with these species has led to increasingly frequent need for sedation and, in some instances, general anesthesia.

DOLPHIN SLEEP

Bottlenose dolphins, like all cetaceans, have an apneustic breathing pattern. Even when resting at the water surface, dolphins take one to three breaths/minute. Each breath is deep, rapidly filling the lungs to 80% or 90% capacity (Ridgway, Scronce, and Kanwisher, 1969). Expiratory flow rates are also very rapid and empty the lung almost completely (Kooyman and Cornell, 1981). Thus, the effort of breathing, even at rest, appears much more pronounced than that of humans and other terrestrial mammals.

Given their need to swim and breathe air with these deep breaths, it is not surprising that many biologists and veterinarians have wondered how dolphins sleep in the water. In the early 1960s John Lilly (1962a) suggested bottlenose dolphins slept with one eye closed and utilized one brain hemisphere at a time; however, he produced no electroencephalograms (EEGs) to support this

hypothesis. Serafetinides, Shurley, and Brooks (1970) reported the first EEG evidence of uni-hemispheric sleep using SC needle electrodes during a one-night recording from a pilot whale (Globicephala scammoni). Mukhametov, Supin, and Polyakova (1977) and Mukhametov (1984) recorded many 24-hour periods from multiple dolphins using screw electrodes inserted through the skull in a multi-channel array with a lownoise wire system that allowed some animal movement around a shallow pool. They demonstrated overwhelming evidence the vast majority of dolphin slow waves were uni-hemispheric and appeared first in one hemisphere and then the other. Remarkably, each hemisphere appears to accumulate a separate sleep debt. When one hemisphere was deprived of slow wave sleep for several days, only that hemisphere showed the typical sleep rebound; the non-deprived hemisphere continued to alternate its slow wave sleep in the usual amount (Oleksenko et al., 1992). Since slow waves appeared only very rarely and then very briefly in both hemispheres simultaneously, Mukhametov, Supin, and Polyakova (1977) and Mukhametov (1984) suggested slow waves in both hemispheres is not compatible with respiration.

Using a small implantable telemetry unit, Ridgway (2002) replicated the earlier uni-hemispheric EEG findings and also recorded symmetrical EEG in both hemispheres during thiopental/halothane anesthesia. There were short periods of EEG slow waves in both hemispheres during the un-anesthetized state although slow waves in both hemispheres were not seen during breaths.

From behavioral observations, Lilly (1962b) stated:

In regard to lateralization of the sleep pattern, these animals sleep with one eye closed at a time. The eye closures are 180 degrees out of phase; it is rare to have both eyes closed at once. The accumulated sleep in each eye runs 120 to 140 minutes per day. The sleep

occurs in brief periods between each respiration running from 20 to 40 seconds per eye closure. A dolphin wakes up in order to take each breath.

Extensive behavioral observations were conducted by McCormick (1969) who was able to observe bottlenose dolphins through large underwater viewing windows. He observed dolphins resting at the water surface, virtually immobile, with both eyes closed and breathing in an "automatic fashion" for periods of greater than or equal to 1 hour.

McCormick (1969) also observed, unlike the bottlenose dolphins, the Dall porpoise (*Phocoenoides dalli*) swam continuously without ever stopping to rest or become immobile. Azov porpoises (Phocoena phocoena) in the same family as the Dall porpoises, were observed to swim continuously as well Mukhametov and Polyakova (1981). From these behavioral observations it would be easy to conclude that Dall porpoises and Azov porpoises never sleep. Mukhametov and Polyakova (1981) fitted three of the Azov porpoises with their EEG recording equipment. The animals swam continuously around their pool. Uni-hemispheric slow waves alternated between the hemispheres while the porpoises continued to swim (Mukhametov and Poliakova, 1981). Therefore, stopping to rest or becoming immobile, is not an absolute requirement for sleep. Although bottlenose dolphins and the largest member of the dolphin family, the killer whale, often rest at the surface as described by McCormick (1969), both mother and calf swim constantly for several weeks after the birth (Lyamin et al., 2005). Thus, if mother and calf are sleeping, it must occur while they are continuously swimming.

DOLPHIN GENERAL ANESTHESIA

The physiology of anesthesia is different from sleep, especially in cetaceans. However, the superficial appearance of these two physiological states gives rise to the common comparison of administering general anesthesia with inducing sleep. Although there are many differences, unconsciousness in these two different physiological states is considered somewhat similar to humans and other land mammals. However, the phenomenon of uni-hemispheric sleep in cetaceans makes comparison between sleep and anesthesia not as applicable in these species. Moreover, in all mammals, arousal from sleep by noxious stimuli has a relatively low threshold, whereas arousal from anesthesia is possible only after recovery.

The first attempt to put a dolphin "to sleep" or give general anesthesia was made by Langworthy (1932) who administered ether by a cone held over the blowhole. The dolphin stopped breathing and died. After a number of attempts to employ intraperitoneal barbiturate anesthesia also resulted in dolphin deaths (Lilly, 1962a; Nagle et al., 1964), one group was successful in develop-

ing endotracheal intubation methods and inducing dolphin anesthesia with 70% nitrous oxide (Nagle et al., 1964). Although nitrous oxide was safe, it was inadequate for major surgery. Ridgway and McCormick (1967, 1971) employed halothane and later IV thiopental (pentothal) for induction and halothane for anesthesia maintenance. Other early work in dolphin anesthesia is reviewed in French by Lecuyer (1983).

More recently, propofol (Branson and Gross, 1994) has become the choice for induction followed by intubation and isoflurane maintenance (Linnehan and MacMillan, 1991). When general anesthesia is achieved, dolphins do not breathe and slow waves appear on the EEG of both brain hemispheres (Ridgway, 2002; Howard, Finneran, and Ridgway, 2006). All successful general anesthesia has required intubation and the use of a respirator. A Bird Mark 9 large animal respirator fitted with an apneustic control device (Bird Corp., Palm Springs, CA) has been employed to mimic normal respiration (Nagle et al., 1964; Ridgway and McCormick, 1967, 1971).

Anatomy and Physiology

Specific anatomical and physiological adaptations of the respiratory and cardiovascular systems, although beneficial for a purely aquatic existence, pose challenges to the clinician for sedation and general anesthesia of the cetacean patient. Much of the physiological and anatomical knowledge discussed here was gained from bottlenose dolphins. Fortunately for the clinician, most of the adaptations are well conserved among the other odontocete species commonly encountered in zoos and aquaria.

The most obvious respiratory adaptation is the blowhole, the external nasal opening of cetaceans. It is positioned on top of the head rather than the front of the face as in all other mammals. Immediately ventral and lateral to the blowhole are right and left lateral vestibular sacs. One can readily palpate these sacs by placing a finger through the blowhole directed to the left or the right. The right sac is larger. Paired internal nares are seen below the nasal plug when it opens. The paired nasal cavities, separated by the nasal septum, extend from the nares ventrally along the cranial aspect of the calvarium to the naso-pharynx just above the larynx. This has a beak-shaped structure frequently referred to as a "goosebeak" because of its semblance in shape (Figure 43.1). The goosebeak is an elongation of epiglottal and cricoarytenoid cartilages supported laterally by arytenoepiglottic muscles (Green, Ridgway, and Evans, 1980). It is held in its dorsally oriented position along the dorsal oropharynx by the nasopharyngeal sphincter muscle. Foods, usually swallowed whole, course laterally around the larynx. The larynx is not permanently affixed in this position and it can be displaced voluntarily by the animal when swallowing large food items, and manually by the clinician when intubating the animal. The larynx leads to a short trachea (Figure 43.2).

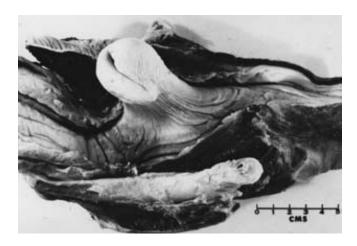


Figure 43.1. The laryngeal "goosebeak" rises from the center of the oropharynx. (From Green RF, Ridgway SH, Evans WE. Functional and descriptive anatomy of the bottle-nosed dolphin nasolaryngeal system with special reference to the musculature associated with sound production. In: Busnel RG, Fish JF, eds. Animal Sonar Systems. New York: Plenum, 1980:199–238, U.S. Navy photograph.)



Figure 43.2. Left lateral view of excised dolphin lung, trachea, and larynx. (U.S. Navy photograph.)

Preceding the carina is a right-sided accessory bronchus (Green, 1972), an important consideration for intubation because it is required for inflation of a portion of the right lung.

Compared with terrestrial mammals, cetaceans have more extensive pulmonary supportive structures. These include complete tracheal and bronchial cartilaginous rings that extend beyond the mainstem bronchi into deep bronchioles, and plates and rings of cartilage that extend all the way to the junctions of alveoli. Smoothmuscle sphincter-like narrowings occur at the terminal bronchioles (Simpson and Gardner, 1972). The lungs contain a great amount of elastic tissue. A dense elastic visceral pleura 1 mm or so in thickness covers each non-septate, non-segmented lung (Figure 43.2). Since cetaceans must be intubated and ventilated for general anesthesia, the anatomy relative to the endotracheal intubation process is especially important.

As mentioned, cetaceans have a specialized respiratory cycle with short, rapid exchange phases followed by long inspiratory apneustic plateaus. They take fewer and

deeper breaths than their terrestrial counterparts. Bottlenose dolphins breathe an average of 2 to 3 per minute and have a tidal volume of 5 to 10 L, representing greater than or equal to 80% of their total lung capacity (Ridgway, 1972).

Anatomic adaptations of the cardiovascular system to support deep diving, long breath holds, and temperature conservation in the cold ocean include large, distensible veins, venous sinuses, venous valves in the lungs, portal triads of the liver, and a venous sphincter in the common hepatic vein at the junction of the inferior vena cava below the diaphragm. A rete mirabile, a highly developed meshwork of arteries and veins between the thoracic vertebral bodies, and periarterial venous rete represent temperature countercurrent exchange systems. These allow cetaceans to peripherally vasoconstrict and still perfuse the brain with warm, oxygenated blood even under the great pressure and temperature extremes experienced at depth (McFarland, Jacobs, and Morgane, 1979). Finally, cetaceans have a profound respiratory sinus arrhythmia that is normal; the heart rate speeds up with each breath and slows between breaths (Figure 43.3).

Physical Restraint

Physical restraint of small cetaceans is common practice. However, it requires multiple personnel and can result in injury to both people and patient owing to the substantial size and strength of most small cetaceans. Therefore, it is recommended physical restraint be performed under the supervision of trained, experienced personnel. However, because experience with cetacean sedation and anesthesia is still relatively limited, most if not all clinically relevant procedures are, and have been, performed with physical restraint alone.

Animals requiring individual care are separated from pool mates either under voluntary control, or with nets or stranding devices. Care is taken when introducing a net into the water; if animals become entangled they must be quickly assisted to the surface so that they can breathe. Many facilities have medical pools to strand animals out of the water for clinical procedures without the need for nets, slings, or stretchers. Clinical procedures have been performed on dolphins and other odontocetes with animals suspended out of the water in fitted slings (Figure 43.4), suspended in water tight boxes, or most commonly, supported out of the water on a soft foam rubber pad on the ground or a large animal surgical table. When not suspended in stretchers or slings, animals are commonly positioned on closed-cell foam padding, with personnel placed on both sides of the animal, one or two people restraining the animal's tail flukes, and one or two people positioned near the animal's head. For animals that are relaxed, simple support of only one or two people may be all the restraint that is required. For more fractious animals, multiple people are needed to provide adequate restraint.

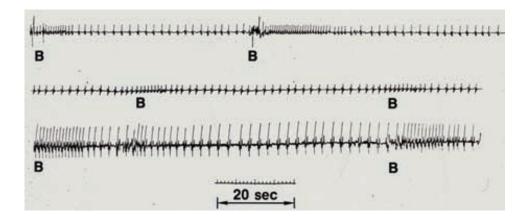


Figure 43.3. A recording of dolphin heart rhythm. Each breath is indicated by the letter B on the recording. With each breath the heart rate increases then slows in a marked sinus rhythm of tachycardia/bradycardia. This rhythm is abolished with the induction of anesthesia.



Figure 43.4. A dolphin is lifted from its pool in a fitted sling. (U.S. Navy photograph.)

Because of the challenges associated with physical and chemical restraint, operant conditioning and training have been used in small cetaceans to encourage them to participate voluntarily in many clinical procedures (blood sampling, ultrasound, radiographs, and endoscopy).

Whenever a cetacean is out of the water, its skin must be kept moist for temperature control and prevention of drying. Special attention is paid to the eyes. To prevent injury or drying during anesthesia it is best to apply a lubricating ophthalmic ointment. Special tables (Figure 43.5) or tanks (Figure 43.6) have been constructed to maintain the dolphin patient in proper position for monitoring and surgery.

Vascular Access Sites

There are several sites for venipuncture, few for drug and fluid administration, and only one proven for repetitive catheterization.



Figure 43.5. Prior to induction of anesthesia, a dolphin rests on a special table held loosely by seat belt straps. (U.S. Navy photograph.)

Dorsal and Ventral Fluke Periarterial Vascular Rete

The ventral fluke periarterial vascular rete (PAVR) is most commonly used for routine venipuncture in odontocetes (Ridgway, 1965). Captive dolphins are frequently trained to allow venipuncture at this site under voluntary stimulus control. Blood is collected with needles ranging from 19 to 23 g and 2 cm (3/4 inch) to 4 cm (1.5 inch). Intravenous antibiotics and fluids can be administered into this site, but the size and microanatomy of the vessel, the accuracy of the needle stick, and the dynamic nature of the peripheral blood vessels limit successful administration. Blood from this site (Figure 43.7) is most commonly venous or an arterial-venous admixture.

Peduncle Periarterial Vascular Rete This venipuncture site is located on the ventral aspect of the terminal vertebral bodies. Injection landmarks are the ventral

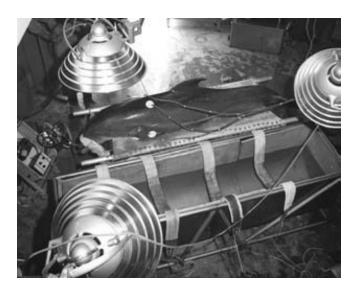


Figure 43.6. The dolphin is anesthetized and ventilated with a Bird respirator through an oral endotracheal tube. White rubber suction cups hold surface electrodes for monitoring the electrocardiogram (ECG). The suction cups provide insulation for the electrodes to allow for recording of the ECG while the animal is immersed. The dolphin will be supported by the warm water and padded straps in the adjacent tank during the surgical procedure. Intravenous fluid is given through the caudal vascular bundle. Blood transfusions, if needed, may be given through the same site or via the periarterial vascular rete. For long procedures, a nebulizer is placed in the line for humidification of respiratory gas. (U.S. Navy photograph.)



Figure 43.7. A 20-g butterfly needle is used to collect a blood sample from the fluke blade. (U.S. Navy photograph.)

peduncle ridge, immediately proximal to the confluence of the right and left fluke PAVR. Venipuncture is performed with needles longer and larger than those used for fluke vessel venipuncture in the same animal. Eighteen to 21 g, 4 to 5 cm (1.5–2 inch) needles and larger may be required. The site is accessed from voluntary fluke presentations or animals out of the water for examinations and procedures (Figure 43.8). The larger arterial diameter at this site allows for rapid collection of large volumes of arterial and arterial-venous admixed



Figure 43.8. Blood is collected from the peduncle periarterial vascular rete (PAVR) employing a 20-g needle and Vacutainer tube. The peduncle PAVR is the best peripheral site for collecting arterial samples. (U.S. Navy photograph.)

blood. It also mitigates some of the challenges encountered with fluid and drug administration at other sites, making it appropriate for intravenous (IV) injection. Assuming appropriate positioning and if necessary restraint of the flukes, the needle may be left indwelling during longer procedures for constant rate infusion of fluids, as well as repeat blood samples for arterial blood gases. Arterial blood pressure has been measured at this site (Ridgway, McCormick, and Wever, 1974); however, needle placement and movement is carefully monitored because shifts may lead to values that are not necessarily reflective of the patient's status.

Dorsal Fin Periarterial Vascular Rete A challenging venipuncture site in smaller cetaceans, it is useful for killer whales (Figure 43.9). In dolphins, it is reserved typically for fractious animals that will not allow access to the flukes or peduncle and as a second site for blood collection during anesthesia or sedation. The dorsal fin PAVR has the same anatomical challenges as the fluke PAVR (Rommel and Lowenstine, 2001). When considering IV drug administration, it is important to remember blood from this site flows directly to a rete around animal's gonads. The authors typically access this site with needles similarly sized to those used for fluke PAVR venipuncture.

Hemal Arch/Caudal Vascular Bundle The caudal vascular bundle runs longitudinally along the ventral midline of the caudal vertebral bodies within an arch formed by the chevron bones. In an adult bottlenose dolphin, a 9-cm (3.5-in.) spinal needle is advanced transversely into the ventral intervertebral space, ventral, and parallel to the lateral processes of the caudal vertebral bodies in the mid- to caudal peduncle region.



Figure 43.9. Accessing the dorsal fin periarterial vascular rete is much easier in larger animals such as the killer whale. (U.S. Navy photograph.)

The caudal vascular bundle is a low pressure, mostly venous system. This site can be catheterized (Van Bonn et al., 1996) and is appropriate for IV fluid and drug administration. However, this is a venous rete and rates of drugs and fluid absorption are variable compared to other sites.

Common Brachiocephalic Vein The common brachiocephalic vein (CBV) (Figure 43.10) is not part of a PAVR. As such, it is an appropriate site to collect purely venous blood samples and measure venous blood pressure. It is also large enough for indwelling catheterization, improving anesthetic monitoring and support capabilities. Drugs and fluids delivered into the CBV may be more rapidly distributed into the general circulation. Thus, they have a more consistent effect than those injected IV into other peripheral sites that are part of PAVRs. Access to the brachiocephalic vein is challenging. In bottlenose dolphins it lies 10 to 12 cm deep under skin, blubber, and muscle, and runs in a transverse plane. The actual site for access is large; 2 to 3 cm wide and 2 cm thick. However, slight misdirection at the skin translates into significant misdirection of the long needles at the level of the vessel. Furthermore, the transverse orientation of the vessel makes catheterization difficult.

The authors have had the greatest success accessing the common brachiocephalic vein with ultrasound guidance. As such, the procedure benefits from two people working together; one person controls the probe and holds the image steady, whereas the other performs the venipuncture. To catheterize the vessel we pass a 14-g, 16-cm needle into the vein, and then feed a 60-cm polyurethane catheter through the needle to a depth of approximately 25 cm. For short-term access (IV drugs, bolus fluids) we use a needle and no catheter. The stylet from an equine 16-g, 14-cm (5.5-in.) radio-opaque catheter is the sharpest disposable needle currently

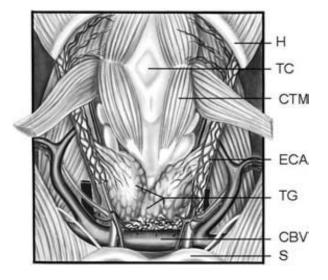


Figure 43.10. Drawing from a dissection of the ventral neck of a bottlenose dolphin. Note that the ECA is covered by a meshwork of veins. CBV, common brachiocephalic vein; CTM, cricothyroid muscle; ECA, external carotid artery; H, hyoid; S, sternum; TC, thyroid cartilage; TG, thyroid gland. (Drawing by Barbara Stolen Irvine from Ridgway SH, Patton GS. Dolphin thyroid: Some anatomical and physiological findings. Z vergl Physiologie 1971;71:129–141.)

available. The animal is always placed in lateral recumbency for the procedure. We have recent evidence placing the animal in right lateral recumbence is more anatomically appropriate for catheterization. Right lateral recumbency, along with the natural tendency of the phlebotomist to orient the needle tip toward the floor, promotes feeding the catheter toward the heart (with left to right flow in the vessel). This is in contrast to feeding toward the venous return from the rete (against flow), as happens with the animal in left lateral recumbency. However, successful catheterization can also be performed with the animal in left lateral recumbency.

Endotracheal Intubation

Endotracheal intubation of adult bottlenose dolphins and larger odontocete species is performed most commonly with an oral approach to the larynx (Figure 43.1). This is accomplished either when the animal is awake (in an emergency situation) or following sedation or induction to anesthesia. Large animal endotracheal tubes with inflatable cuffs (16-30 mm ID) are appropriate for most adult bottlenose dolphins. Intubation frequently requires multiple personnel; one or more people to hold the animal's mouth open with soft rolled towels and another to pass the endotracheal tube. The oral approach is blind, and requires manual removal of the larynx (goosebeak) from the nasopharyngeal sphincter to orient it in a rostral direction. Two fingers are then placed in the glottis (Figure 43.1) and the endotracheal tube guided into the trachea. In most odontocetes the trachea is very short (Figure 43.2), and there is a right-sided accessory bronchus (Green, 1972) that

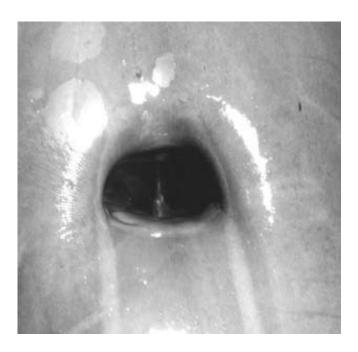


Figure 43.11. Dolphin open blowhole. Anterior is down in this photograph. The nasal septum divides the nares so that only a small tube can be inserted down one nostril through the nasal cavity to reach the glottis sitting below the opening of the distal nares (see also Figures 43.1 and 43.2). (U.S. Navy photograph.)

precedes the carina. Care is taken not to advance the endotracheal tube too far and block the separate right bronchus.

Tracheal intubation through the oral cavity is not possible in some small odontocetes owing to their small mouths and oropharynx. Intubation in these animals is accomplished through the blowhole (Figure 43.11) with a small tube. This approach is more complicated owing to redundant tissue and muscular folds, used for vocalization and echolocation, encountered between the goosebeak and the blowhole. The tube is inserted through the right or left nasal cavities, limiting the diameter used. Intubation is facilitated by a bronchoscope to visualize the goosebeak and a stylet to advance the endotracheal tube through the glottis. A potential complication of prolonged (several hours) blowhole intubation is dysfunction once the animal is back in the water. To our knowledge, prolonged anesthesia with blowhole intubation has not been performed.

Blowhole intubation was used in small dolphins (*Stenella* styx and *Delphinus delphis*) under experimental conditions at sea (Rieu and Gautheron, 1968). Xylocaine (2%) was injected through the tube to produce laryngeal anesthesia.

Monitoring and Supportive Care

Anesthetic monitoring and support is as critical in cetaceans as terrestrial mammals. Spontaneous ventilation, circulation, and perfusion in cetaceans normally occur with the animal's body weight supported by the

buoyancy forces exerted by the water column. Removing the animal from water for a clinical procedure incurs a cardiopulmonary disadvantage. A collapsible thorax, gravity, and the animal's mass combine to increase respiratory effort and compress muscles and vessels. Changes in temperature and pressure may cause hyperthermia or hypothermia, abnormal vasoconstriction, or vasodilation with resultant blood shunts. Respiratory, cardiovascular, or central nervous system depressing drugs exacerbate cardiopulmonary compromise.

A comprehensive approach to monitoring and support of the cetacean patient is applied. Since reported drug protocols are frequently limited to experience with only a few animals, the anesthetist should always be on alert for the possibility of profound and unexpected drug reactions. Applying anesthetic monitoring equipment to unsedated, out of water patients is as important as for the anesthetized patient. This can be for no other reason than it can help build the clinician's familiarity with individual animals' normal heart and respiratory rates, core temperatures, and reflexes.

Respiratory support in sedate animals that are still ventilating spontaneously is not necessary. However, many marine mammal clinicians still provide supplemental oxygen to dolphins and whales that are out of the water or sedate. For general anesthesia in dolphins, successful mechanical ventilation has been performed with a Bird Mark 9 respirator with an apneustic plateau modification for prolonged inspiratory hold in the ventilation cycle. A respiratory rate of 2 to 4 breaths per minute (Ridgway and McCormick, 1967, 1971; Ridgway, McCormick, and Wever, 1974) is generally used. Early experiences suggested general anesthesia greater than or equal to 4 hours without this modification resulted in reduced alveolar inflation and lung expansion, with associated respiratory acidemia and cardiovascular depression (Ridgway and McCormick, 1971). One recent report suggests the apneustic plateau ventilatory cycle is unnecessary for shorter procedures (Reidarson, 2003). In our recent experience, a *Tursiops* anesthetized with isoflurane for 2 hours showed lower end-tidal CO₂ levels (45-50 mmHg), that more closely approximated the animal's non-anesthetized expiratory CO2, when ventilated without the apneustic plateau. Monitoring endtidal carbon dioxide (ETCO₂) as an indicator of adequate ventilation and perfusion is recommended for anesthetized dolphins, and even dolphins under sedation (not intubated). For sedate animals, the sampling probe is held in the air stream above the blowhole. End-tidal CO₂ measurements are calibrated against the patient's pCO₂ to determine how representative the measured values are of true alveolar CO_2 .

Blood gases are measured as in other animals, and normal ranges are similar to those in other mammals. Because of cetacean vascular anatomy, collecting a purely arterial or purely venous sample is possible, but less likely than collecting an arteriovenous admixture when

sampling from peripheral sites. A truly venous sample is collected from the brachiocephalic vein as described. In the authors' experience the best peripheral site for a pure arterial sample is the peduncle PAVR.

Heart rate is monitored with electrocardiogram leads as in other species. The authors recommend placing the leads before the animal has received any drugs to establish baseline readings. Normal, stable animals have a profound resting sinus arrhythmia (Figure 43.3). However, animals that are anxious or stressed will override the arrhythmia and maintain a steady, mildly tachycardic rate (100–120 bpm). Additionally, general anesthesia results in abolition of the sinus arrhythmia (Ridgway, 1972; Ridgway, McCormick, and Wever, 1974). Published reports suggest a heart rate less than or equal to 60 bpm is cause for concern in anesthetized dolphins (Ridgway and McCormick, 1971).

Hemoglobin saturation is indirectly measured with a pulse-oximeter probe placed on the tongue of anesthetized patients (Linnehan and MacMillan, 1991). In sedated animals, the authors have attempted to place reflectance probes rectally and within the genital slit with little success in obtaining readings.

Mean arterial blood pressure (MAP) has been reported in bottlenose and pacific white-sided dolphins (Ridgway and McCormick, 1971; Ridgway, McCormick, and Wever, 1974). These measurements were recorded from an indwelling needle within the ventral peduncle PAVR. The authors have also successfully measured central venous pressure (CVP) in several bottlenose dolphins through an indwelling IV catheter placed in the common brachiocephalic vein.

Body temperature is monitored with a flexible thermometer probe placed rectally (Figure 43.12) to a depth of 15 to 25 cm depending on animals size (Nagel, Morgane, and McFarland, 1964; Ridgway, 1965; Ridgway and McCormick, 1967; Ridgway, McCormick, and



Figure 43.12. A flexible probe from an electronic thermometer is inserted 15 to 25 cm into the rectum, depending on the animal size, to measure temperature. (U.S. Navy photograph.)

Wever, 1974). Clinicians should be aware that countercurrent heat exchanges systems for internal gonads may interfere with thermometer readings if the probe is placed too deep or too shallow, and lead to misinterpretation of core body temperature readings (Rommel, Pabst, and McLellan, 1992, 1993).

Depth of anesthesia is determined by assessment of reflexes as in other mammals. Palpebral and corneal responses, response to manipulation of the blowhole, jaw-tone, and swallow reflexes are all appropriate. Ridgway and McCormick (1967) reported loss of swimming motion in the tail flukes may be the most reliable indicator a surgical anesthetic plane has been reached. Future advances in assessing anesthetic depth may be achieved through EEG monitoring and use of the bispectral index (Howard, Finneran, and Ridgway, 2006).

Field Techniques and Strategies

Because of limited experience and serious potential complications associated with the use of sedatives in small cetaceans, most field work is accomplished with animals physically, rather than chemically, restrained. There are to date no peer-reviewed publications showing data for sedation of cetaceans in a field setting. However, there is ongoing work and analysis to attempt sedation of entangled great whales to improve rescuers' chances of disentangling these large animals. New data should be forthcoming as various teams work to improve methods of drug delivery and animal support.

Body Weight

Body weights vary with age, class, sex, and species. Adult weight ranges of the commonly encountered cetacean species are listed in Table 43.1. Cetaceans are relatively large, with large body mass, and therefore may require a large drug dose. For many pharmaceuticals a direct extrapolation of mg/kg dosage is appropriate. However, for sedative and anesthetic drugs consideration of dosage scaling and basal metabolic rate must be made. In the author's experience, larger cetacean species require smaller drug dosages (mg/kg basis) than smaller species to achieve the same level of sedation. As mentioned, most anesthetic and sedative drug use in cetaceans is limited to a very small sample size. As such,

Table 43.1. Common juvenile and adult weight ranges for selected species of cetaceans housed in oceanaria and aquaria.

Species	Weight Range (kg)
Lagenorhynchus obliquidens	60-160
Tursiops truncatus	90-315
Orcinus orca	500-5600
Delphinapterus leucas	300-1600
Pseudorca crassidens	430-800

the potential for unpredictable drug reactions, even from published dosages, exist.

Analgesia

If there are little published data on anesthetic drugs used in cetaceans, there are even less for analgesics. The greatest challenges to cetacean pain management are the difficulty in effective assessment of pain in measuring response to therapy, and assessment of potential drug reactions. Several marine mammal clinicians have encountered acute, negative side-effects after the use of non-steroidal anti-inflammatory drugs in cetaceans (McBain, personal communication). With that caveat, Table 43.2 lists several analgesic and anti-inflammatory agents that have been used.

Anesthetic and Sedative Drugs

Drugs previously reported or used by the authors for sedation and local or general anesthesia of several cetacean species are presented in Tables 43.2 and 43.3. The authors' caution in most instances the number of animals exposed to these drugs is small, and the potential for unpredictable or as yet unrevealed drug reactions is not insignificant. We estimate general anesthesia in cetaceans has been performed less than 100 times. However, animals have been safely, and in some instances repetitively, sedated or anesthetized with the listed drugs. Benzodiazepines and opioids are most commonly used for sedation. Diazepam as an oral drug for light sedation and midazolam as an injectable are frequently employed. Diazepam (0.55-0.60 mg/kg orally) has been used to help trained dolphins remain still for 35 or 45 minutes for functional scans such as positron emission tomography (Figure 43.13). In the case of overdosage, flumazenil is given orally (Votey et al., 1991) or IV depending on the urgency (Geller et al., 1988; White et al., 1989). Meperidine is not infrequently used, but for some clinicians may be superseded by butorphanol (Table 43.3). Several marine mammal clinicians are developing a growing comfort level with butorphanol (Chittick et al., 2006) as a sedative drug that provides analgesia, safe light sedation, and is easily



Figure 43.13. A trained dolphin remains still for a PET scan following 0.55 to 0.60 mg/kg of oral diazepam. The animal is kept moist with sponges and spray bottles during the 35- to 45-minute procedure (Ridgway SH. Houser D, Finneran JJ, et al. Functional imaging of dolphin brain metabolism and blood flow. J Exp Biol 2006;209:2902–2910.) (U.S. Navy photograph.)

Table 43.2. Analgesic drugs used in cetaceans.

Category	Drug Name	Species	Dosage	Route	Comments	Reference
NSAIDs	Flunixin Meglumine (Banamine)	Tursiops truncatus, Orcinus orca	0.25–0.5 mg/kg SID	IM	Caution with use in cetaceans as gastric ulcers are common	McBain, personal communication
	Carprofen	Tursiops truncatus	0.5 mg/kg SID	PO	Gastric ulceration seen	Schmitt, personal communication
	Acetaminophen	Tursiops truncatus, Orcinus orca	3–5 mg/kg SID	PO	Monitor transaminases	Walsh, personal communication
Opioids	Butorphanol	Tursiops truncatus, Orcinus orca	0.05-0.15 mg/kg	IM	Possible excitatory response seen in one dolphin	Chittick et al., 2006
	Tramadol	Multiple (bottlenose dolphin, common dolphin, rough tooth dolphin, spinner dolphin, spotted dolphin, and pygmy and dwarf sperm whales)	0.1–0.4 mg/kg BID	РО	Titrate up to least effective dose. Produces good analgesia without analgesia change in appetite. Drowsiness seen at 0.73 mg/kg [Can be used IM or IV as well]	Manire, personal communication, 2006

Table 43.3. Chemical sedative and anesthetic agents used in Bottlenose dolphins (*Tursiops truncatus*).

Category	Drug Name	Dosage	Route	Comments	Reference
Premedication	Atropine	0.02 mg/kg	IM		Ridgway and McCormick, 1971
Sedatives	Diazepam	0.1–0.2 mg/kg 0.25–1.0 mg/kg	IM PO	Larger doses reserved for research or for animals that may have become refractory to smaller oral doses of diazepam. Keep flumazenil available.	Reidarson, 2003 Ridgway et al., 2006 Howard et al., 2006
		0.26-0.36 mg/kg	PO	neep numuzem uvumuze.	Schroeder et al., 1986
	Chlordiazepoxide	0.5 mg/kg	IM	Reduces anxiety, useful for shipping, no harmful side effects	Geraci and Sweeney, 1986
	Midazolam	0.05-0.15 mg/kg	IM	Provides good plane of sedation lasting about 45–60 minutes. Higher dosages should be investigated.	McBain and Walsh, personal communication Ridgway and Dold, personal observation
	Flumazenil	0.005 mg/kg	IM, PO, IV, sublingual	Can be given at equal volume of midazolam when midazolam is 5 mg/ml and flumazenil is 0.5 mg/ml. Usually titrate dose.	McBain and Walsh, personal communication Ridgway and Dold, personal observation
	Butorphanol	0.05-0.15 mg/kg	IM	Sedation adequate for bronchoscopy and minor procedures. Possible reactions seen when combined with bronchodilators.	Chittick et al., 2006
	Meperidine	0.1-2.0 mg/kg	IM	Given in combination with midazolam can produce deep level of sedation that is reversible.	Joseph and Cornell 1988; Reidarson 2003; Ridgway, 1965
	[Naloxone]	5–10 mg/kg	IM/IV	Butorphanol and meperidine reversal	Reidarson, 2003
	[Naltrexone]	0.005 mg/kg	IM/IV	Opioid reversal	Chittick et al., 2006
Induction agents	Ketamine Medetomidine	1.75 mg/kg 10–40 mg/kg	IM IM/IV	Single case only Abolishes sinus arrhythmia and causes respiratory depression, decreased central venous pressure	Reidarson, 2003 Reidarson, 2003 Ridgway and Dold, personal observation
	[Atipamezole]	50-200 mg/kg	IM/IV	Equal volume of medetomidine for reversal; medetomidine is 1 mg/mL and atipamezole is 5 mg/mL	Ridgway and Dold, personal observation
	Thiopental	10-15 mg/kg	IV	Requires additional inhalant anesthesia for full induction	Ridgway and McCormick, 1971
	Propofol	0.5–3.5 mg/kg	IV	Onset and duration of effect injection site dependent	Linnehan and MacMillan, 1991; Ridgway and Dold, Van Bonn, personal communication
Inhalational agents	Halothane	0.5%-3.5%	IH	Higher dose for induction, lower maintenance dose	Ridgway, 1965; Ridgway and McCormick, 1967, 1971; Medway et al., 1970
	Isoflurane	0.5%-2.0%	IH	Higher dose for induction, lower maintenance dose	Linnehan and MacMillan, 1991; Ridgway and Van Bonn, personal observation, 1991–2005 Dover et al., 1999
	Nitrous oxide	70%	IH	Light anesthesia	Nagel et al., 1964

reversed with naloxone or naltrexone. Thiopental and propofol have been used for induction to general anesthesia. Reidarson (2003) reports the use of ketamine/medetomidine for successful intubation and maintenance of anesthesia in one animal. The authors

have limited experience with medetomidine, and with ketamine in only one patient (SR). In the author's experience, medetomidine alone produces significant respiratory and central venous pressure depression, in addition to light sedation. The effects are reversed with

atipamezole. Anesthesia has been maintained with the use of the inhalant anesthetics halothane (Ridgway, 1965; Ridgway and McCormick, 1967, 1971) and isoflurane (Linnehan and MacMillan, 1991; Dover et al., 1999; Haulena and Heath, 2001). Isoflurane is currently the inhalant of choice in cetaceans (SR). However, sevoflurane deserves consideration, because recovery of humans was faster with sevoflurane anesthesia compared with isoflurane following induction of anesthesia with propofol.

Recovery

Perhaps greater than the challenges posed by induction and maintenance of general anesthesia are those encountered upon recovery. Owing, in part, to the difficulty of determining anesthetic depth, and also the replacement of the goosebeak as a necessary step for voluntary ventilation, great care is taken as one attempts to recover the animal and get it breathing on its own.

LOCAL ANESTHESIA

Two percent Xylocaine (Lidocaine HCl) has frequently been used for SC infiltration for surface surgical procedures. Blocking the infra-alveolar nerve, a branch of the mandibular nerve, with Xylocaine infiltration has been effectively employed for dental procedures (Ridgway, Green, and Sweeney, 1975).

DISEASE ISSUES

Given their anatomy and physiology, cetaceans are particularly susceptible to lung disease; pneumonia is the most commonly diagnosed severe disease in these species. Since these animals mask disease (Geraci and Sweeney, 1986), a high index of suspicion is maintained; animals showing evidence of disease may have some loss of normal pulmonary function and, accordingly, may have a potential for decreased oxygenation.

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44

Sirenians (Manatees and Dugongs)

Elizabeth J. Chittick and Michael T. Walsh

TAXONOMY AND BIOLOGY

Distributed throughout fresh, brackish, and marine tropical waters of North and South America and Africa, three species of manatees (*Trichechidae*) and one species of dugong (Dugongidae) comprise the family Sirenia (Table 44.1) (Domning and Hayek, 1986; Reynolds and Odell, 1991). Genetically related to elephants (Probosicidae) and hyrax (Hyracoidea), these hind gut fermenters are the sole obligate herbivores of the marine mammal world. Manatees are considered "weakly" social species, establishing no long-term bonds other than mother-calf pairs and forming only temporary congregations of individuals during winter months at warm water sites or when breeding (Hartman, 1979; Reynolds, 1981; Wells, Boness, and Ratheun, 1999; Odell, 2003). Calves generally stay with their mothers for 1 to 2 years, and reach sexual maturity at 2 to 5 years of age (United States Fish and Wildlife Service, 2001; Odell, 2003). In comparison, dugongs take approximately 9 to 10 years to reach sexual maturity and are often found in large herds with "amorphous" social organization, the only close identifiable social bonds being those between mother and calf (Wells, Boness, and Ratheun, 1999; Odell, 2002).

Because of habitat loss, human interaction problems, and natural disease in their home ranges, sirenians are currently listed under CITES Appendix I or II and the IUCN Red List (Reynolds and Odell, 1991; Baillie, Hilton-Taylor, and Stuart, 2004). The United States Endangered Species Act categorizes West Indian and Amazonian manatees and dugongs as endangered, and the West African manatee as threatened (United States Fish and Wildlife Service, 2001). Mortality associated with human interaction either owing to hunting, boat injury, or habitat loss, is believed to have had significant impacts on sirenian populations in general (Reynolds and Odell, 1991; Odell, 2003). Current conservation efforts for sirenians include worldwide public education

campaigns, local and national legal protection, and rescue and rehabilitation programs.

Medical advancements in the care of rescued sirenians have improved survivability and potential for reintroduction to the wild. The use of sedative agents was first applied in Florida manatees in the late 1980s and general anesthesia first attempted in 1990 (Walsh et al., 1997). Anesthesia of manatees and dugongs is still an emerging field. However, much has been recently learned to effectively sedate, anesthetize, and treat these species. The information presented in this chapter focuses predominantly on the West Indian manatee, but likely has applications across the Sirenia family.

ANATOMY AND PHYSIOLOGY

Sirenians have a somewhat tubular body shape and a wide dorsoventrally flattened fluke that is paddle-shaped in manatees and bilobed in dugongs. Whereas manatees tend to have more dorsoventrally flattened bodies, dugongs are more laterally compressed, particularly caudally. Sirenian skeletons are comprised of dense pachyostotic bone (Fawcett, 1942a). They have relatively short but mobile pectoral flippers and lack hind limbs. Flippers of male manatees are longer in length than those of females, and have more roughened epithelium medially, which likely aids in holding a female during copulation. Male manatees also tend to weigh less than females and have leaner body composition.

The skin of manatees is generally thick, tough, and sparsely haired, with the exception of the Amazonian manatee, which has smooth skin (Domning and Hayek, 1986; Reynolds and Odell, 1991). Nill et al. (1999) found the increased collagen network of the manatee dermis is roughly $2.5 \times$ denser than that of terrestrial mammals. This unique skin density, along with their pachyostotic bones, helps counterbalance the positive buoyancy effects of the air-filled lungs and intralumenal gas of the

Table 44.1. Family Sirenia.

Genus and Species	Common name	Length ^{a,b}	Mass ^b	Distribution
Dugong dugon	Dugong	Adults: 2.7 m avg., upto 3.3 m Calves: 1–1.3 m	Adults: 250–300 kg avg, up to 400 kg Calves: 20–35 kg	Coastal waters of Indo–Pacific
Trichechus senegalensis	West African manatee	Adults: 3–4 m	Adults: <500 kg	Coastal waters, rivers, and lakes of west- central Africa
Trichechus inunguis	Amazonian manatee	Adults: 2.8–3 m Calves: 0.8–1 m	Adults: 450–480 kg Calves: 10–15 kg	Freshwater rivers and lakes of Amazonian basin
Trichechus manatus	West Indian manatee (2 subspecies)			
T.m. manatus	Antillean manatee	Adults: 1.85–2.7 m, up to 3.5 m	Adults: max 1,000 kg	West Indies, Caribbean, coastal waters and rivers of Mexico, Central America, northeastern South America
T.m. latirostris	Florida manatee	Adults: 2.7–4 m, avg 3 m Calves: 1.2–1.4 m	Adults: 400–1,775 kg, avg 400–600 kg males, max 1,600 kg females Calves: 18–45 kg, avg 30 kg	Coastal waters and rivers of southeastern United States

From Domning DP, Hayek LAC. Interspecific and intraspecific morphological variation in manatees (Sirenia: *Trichechus*). *Mar Mamm Sci* 1986;2:87–144; Reynolds JE III, Odell DK. *Manatees and Dugongs*. New York: Facts on File, Inc., 1991:1–192; Converse LJ, Fernandes BS, MacWilliams PS, et al. Hematology, serum chemistry, and morphometric reference values for Antillean manatees (*Trichechus manatus manatus*). *J Zoo Wildl Med* 1994;25:423–431; Nowak RM. *Walker's Mammals of the World*, 6th ed. Baltimore: Johns Hopkins University Press, 1999:982–992; Walsh MT, Bossart GD. Manatee medicine. In: Fowler ME, Miller RE, eds. *Zoo & Wild Animal Medicine, Current Therapy*, 4th ed. Philadelphia: W.B. Saunders, 1999:507–516; Odell DK. Sirenian life history. In: Perrin WF, Würsig B, Thewissen JGM, eds. *Encyclopedia of Marine Mammals*. San Diego: Academic Press, 2002:1086–1088; Murphy D. Sirenia. In: Fowler ME, Miller RE, eds. *Zoo and Wild Animal Medicine*, 5th ed. St. Louis: Elsevier Science, 2003:476–482.

^aStraight length, snout to tail tip.

^bCalf length and mass ranges at time of birth.

gastrointestinal tract in these animals (Nill et al., 1999; Kipps et al., 2002).

Unique sirenian facial features include small eyes, which close by a sphincter rather than upper and lower eyelids, a flexible upper lip and an oral disk covered with modified vibrissae for use when foraging, and nostrils with valves that close between breaths. Dentition varies between manatees and dugongs. Although manatees horizontally replace their molars throughout life, dugongs do not. In addition, manatees lack functional incisors and premolars, whereas dugongs have both premolars and small tusk-like maxillary incisors (Reynolds and Odell, 1991). In place of incisors, manatees have a dorsal dental pad that articulates with the lower jaw just caudal to a firm gingival ridge overlying the symphysis of the mandible. Because of manatees' relatively small mouth, laterally narrowed oral cavity, thick short tongue, and elongated soft palate, oral visualization of the glottis is very difficult. Even with maximal distention of the jaws in adult manatees, the glottis can not usually be seen.

The manatee trachea is relatively short and bifurcates at the thoracic inlet into two separate pleural cavities or hemithorax. The specialized diaphragm of

sirenians has a transverse septum separating the heart and lungs from other organs, as well as two hemidiaphragms that horizontally extend the length of the body and divide the pleural spaces from the abdominal cavity (Rommel and Reynolds, 2000). Unlike other marine mammals, manatee and dugong respiratory tracts comprise the dorsal third of their body cavity, extending from the shoulders to the pelvis and remaining dorsal to the heart (Figure 44.1) (Rommel and Reynolds, 2000). Because of this position of the lungs, intramuscular (IM) injections are placed in the gluteal muscles to avoid injury to organs under more cranial epaxial musculature. Another consideration with regard to the respiratory system of sirenians is the position of the gastrointestinal tract, which lies ventral to the thorax and can comprise 23% of an animal's weight (Reynolds and Rommel, 1996). As hindgut fermenters, manatees have a distinct round cecum with two ovoid diverticula and an enlarged colon which aid with digestion of vegetation. In well-nourished animals, the cecum and large intestine together comprise approximately 10% of the body weight in dugongs, and 14% in manatees (Marsh, Heinsohn, and Spain, 1977; Reynolds and Rommel, 1996). The nutritional status of the animal and

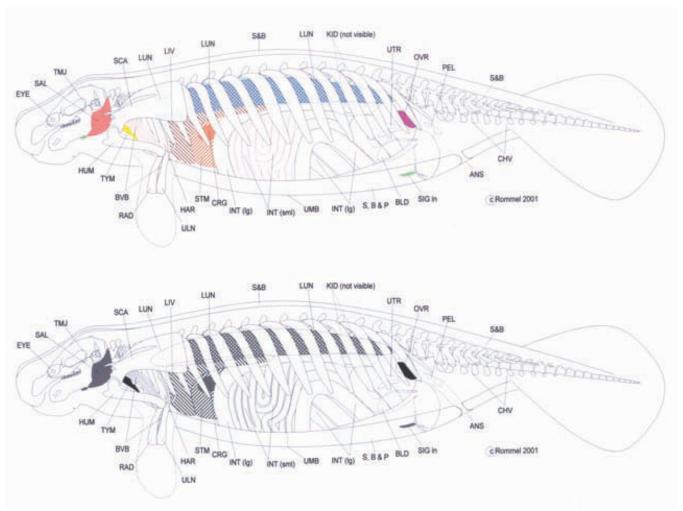


Figure 44.1. Florida manatee (Trichechus manatus latirostris) internal organ position. ANS, anus; BLD, urinary bladder; BVB, brachial vascular bundle; CRG, cardiac gland; CHV, chevrons; EYE, the eye; HAR, heart; HUM, humerus; INT, intestines; KID, left kidney (not visible from this vantage in the manatee); LIV, liver; LUN, lung; OVR, left ovary; PEL, pelvic vestige; RAD, radius; SAL, salivary gland; S&B, skin and blubber; SCA, scapula; SIG In, superficial inguinal lymph node; S,B,&P, skin, blubber, and panniculus muscle, cut at midline; STM, stomach; TMJ, temporomandibular joint; TYM, thymus gland; ULN, ulna; UMB, umbilical scar; UTR, uterine horn; VAG, vagina. (Used with the permission of Dr. Sentinel Rommel.)

the amount of ingesta present in the intestinal tract can influence the respiratory capacity in the awake and sedated animal. When animals are removed from water for anesthetic procedures, pulmonary compression can occur from these internal organs and ventilatory variables must be closely monitored.

Respiratory adaptations for diving in sirenians are similar to those of other marine mammals. The terminal bronchioles of manatees are reinforced with cartilage (Pabst, Rommel, and McLellan, 1999). Inspiration is closely paired with and follows forceful expiration, allowing animals to dive with replenished oxygen stores. Sirenians also have long interbreath intervals, which generally last 2 to 3 minutes in Florida manatees, but can extend as long as 24 minutes in "bottom-resting" individuals (Reynolds, 1981). In studies evaluating the response of Amazonian manatees to hypoxemia and hypercapnia in relation to respiratory drive, carbon dioxide rather than oxygen was concluded to be the

"primary controller of ventilation and dive time" (Gallivan, 1980). Similar to other marine mammal dive responses, dugongs and manatees develop bradycardia; however, it is generally characterized as "sluggish and modest" compared with that of cetaceans and pinnipeds (Scholander and Irving, 1941; Elsner, 1999).

The sirenian heart lies cranioventral to the lungs and anterior to the abdominal organs between the pectoral flippers. The heart rate can often be assessed by evaluating the skin pulse over this area when an animal is in ventrodorsal recumbency. One of the few available vascular access sites in manatees includes a brachial vascular bundle comprised of a rete of veins and arteries in the interosseous space between the radius and ulna (Fawcett, 1942b). This site is accessed from the medial or lateral sides of the pectoral flippers (Figure 44.2A,B). A caudal tail vascular bundle is also available for venipuncture, particularly in younger animals where pectoral vessels are small (Figure 44.3). Care is taken





Figure 44.2. A and B. Brachial vascular bundle venipuncture site in a Florida manatee calf (Trichechus manatus latirostris).

when using this caudal tail site for IV access in unanesthetized animals, because forward thrust of the fluke could injure the phlebotomist. Because of the potential danger from the fluke, this site is generally not used in awake individuals except for compromised neonates.

Unlike other marine mammals, West Indian manatee metabolic rates are 25% to 30% of predicted values and result in their unique warm water thermoregulatory requirements and relative cold intolerance (Irvine, 1983; Worthy, 2001). Amazonian manatees also have relatively low metabolic rates and limited capacity for thermogenesis (Gallivan, Best, and Kanwisher, 1983). Depending on the season, Florida manatees are found in water ranging from 22°C (72°F) to over 32°C (90°F). While manatees may reside in water cooler than 21°C (70°F) during winter months, they have been observed to shiver at these temperatures and develop skin damage in temperatures less than or equal to 16°C (61°F). The degree of damage is dependent on length of cold water exposure, and the animal's nutritional state and size.



Figure 44.3. Caudal tail vascular bundle venipuncture site of the Florida manatee calf (Trichechus manatus latirostris).

Manatees less than or equal to 300 kg are physiologically less adaptable to cold stress than larger manatees; juveniles seem unable to increase their metabolic rates to compensate for cold temperatures less than or equal to 16°C (61°F) (Worthy, 2001). For long-term rehabilitation of manatees, water temperatures are generally maintained greater than 24.5°C (76°F), although often raised to 27°C to 29°C (80-84°F) for neonates, cold-stressed, or thin individuals. The recommended ambient air temperature for animals removed from the water for procedures is 22°C $\,$ to 26°C (72-79°F) (Bossart, 2001). If ambient temperatures drop less than or equal to 20°C (68°F) time for outof-water procedures is minimized to reduce exposure to cooler air. In addition to thermoregulatory impacts, it has been suggested the lower metabolic rate of sirenians has implications for drug metabolism, distribution, and elimination (Murphy, 2003).

PHYSICAL RESTRAINT TECHNIQUES

To minimize injury to an animal or handlers, it is preferred manatees are removed from the water for medical and surgical procedures. Acquisition of sick or injured wild manatees usually involves setting long nets to encircle, then "bag" an animal before pulling it onshore or into a boat. When working with nets in bodies of water, particular care is taken to avoid net entanglement of the animal(s) or personnel that lead to injury or drowning. Hoop netting has limited success with dugongs, and where regulatory and equipment constraints exist for handling this species, a "rodeo method" of capture in shallow open water has been described (Lanyon et al., 2006). Care is taken to minimize injury to animal handlers, as well as reduce dugong chase and handling time, and the potential development of fatal capture stress or myopathy (Marsh

and Anderson, 1983). The authors do not recommend this capture method for manatees.

In captive environments, physical restraint is accomplished using nets or stretchers, dry-docking with pool water drops, or raising a medical pool floor. Whether in captivity or the wild, care is taken during any "catchup" as these animals actively avoid capture and restraint. The strong thrust of sirenian tails and often large body size (Table 44.1) make injury a possibility to both handlers and animals. Only trained personnel participate in the capture and restraint of sirenians.

Although these animals spend their entire lives in water, they are capable of being sustained outside of the aquatic environment for a number of hours. Intermittently spraying with water throughout a procedure helps prevent skin desiccation and overheating, although their skin is much more resistant to drying than cetaceans. When "stranded" for diagnostics or therapeutics, animals are generally placed on closed or open cell foam to cushion their body mass and reduce pressure on internal organs. Animal position is adjusted with stretchers, boat sling straps (placed around the animal's body), cranes, and in smaller animals, manually. When animals are in sternal recumbency, a sheet of closed cell foam is placed over the dorsal aspect of the fluke for handlers to sit on and restrain the tail (Figure 44.4). Handlers also position themselves on either side of the animal to prevent lateral movement. It is not uncommon for manatees to lay quietly either sternally or dorsoventrally during transport or non-painful procedures. Care must be taken around the head and tail areas. Manatees can explosively resist restraint and are capable of touching the tips of their tails to their snouts and/or rolling. Particularly fractious animals are secured to restraint boards or administered sedatives if necessary. In cases of thoracic trauma, where rib fractures exist, manatees are sedated or strapped to a board to minimize further damage to the chest during diagnostic or treatment procedures.



Figure 44.4. Restraint of a Florida manatee (Trichechus manatus latirostris).

ANALGESIC AND ANESTHETIC DRUGS

Reported drugs and dosages are listed in Table 44.2. The relatively low metabolic rate of sirenians may contribute to their apparent sensitivity to sedative and opioid drugs compared with terrestrial mammals (Murphy, 2003). Diazepam and midazolam have been used extensively for both mild and pre-operative sedation. Meperidine has also been used in conjunction with benzodiazepines for more fractious individuals or for procedures that may result in surgical discomfort. In captive environments, after administration of these sedatives, animals are often placed back in shallow water pools to allow the agent to take effect and minimize the effects of restraint overriding the sedative. Sirenians are monitored closely with higher sedative dosages for evidence of hypoventilation or reduced ability to surface to breathe. A combination of detomidine (0.017 mg/kg IM) and butorphanol (0.017 mg/kg IM) resulted in marked respiratory depression in a 700-kg female Florida manatee (Neiffer and Stamper, 2006). IV administration of yohimbine/naltrexone/supplemental atipamezole reversed the respiratory effects. The animal was later sedated with lower dosages of detomidine (0.0085 mg/ kg IM) and butorphanol (0.0085 mg/kg IM) without adverse side effects (Neiffer and Stamper, 2006). Doxapram (IV, IM) has been administered to improve respiration in sedated manatees.

Local infusion of 2% lidocaine at a surgical site is effective, in conjunction with sedation, for analgesia in minor procedures. Epidural administration of 1% lidocaine has been performed once in a manatee undergoing spinal surgery for a vertebral fracture (Bossart, 2001). Other analgesic agents used in sirenians include nonsteroidal anti-inflammatory drugs, but care is taken to avoid gastrointestinal (GI) upset with these drugs by minimizing dosage and frequency of use. IM flunixin meglumide is not used for greater than a few days in succession to avoid GI or renal compromise. Butorphanol has also been administered for analgesia either intra or post-operatively in West Indian manatees.

Sedative or analgesic drugs are administered IM or IV. Onset of drug effects after IM injection is approximately 15 to 20 minutes (Bossart, 2001), although maximum effect may not occur until 25 minutes in some individuals. Because of the thickness of the skin and subcutaneous blubber, needles are advanced perpendicularly and forcefully to reach the deep layers of the lumbar epaxial musculature for injection of sedatives. For adult Florida manatees, 18-gauge 8.75-cm (3.5-in.) spinal needles are used to administer drugs IM, whereas 20- or 21-gauge 3.75- to 5-cm (1.5- to 2-in.) needles are used in calves. The individual administering the drug keeps pressure on the syringe plunger to avoid reflux of sedative back into the syringe. Digital pressure is applied to the injection site to avoid drug leakage after removal of the needle.

Table 44.2. Analgesic, anesthetic, and reversal agents for the Florida manatee (*Trichechus manatus latirostris*).

Agent	Use	Dosage ^a	Comments	Reference
Atipamezole	Reversal	1 mg/20 mg xylazine IV	For xylazine reversal	Murphy, 2003
Butorphanol	Sedative, analgesic	1 mg/2 mg detomidine IV 0.01–0.025 mg/kg IV	For detomidine reversal In combination with diazepam for mild painful procedures, anesthetic induction, give butorphanol	Murphy, 2003 Murphy, 2003
		0.005-0.01 mg/kg IV	10 minutes prior to diazepam In combination with detomidine for minor surgical procedures or anesthetic induction	Murphy, 2003
Detomidine	Sedative	0.005-0.01 mg/kg IM	Moderate sedation, beware of narrow therapeutic index	Murphy, 2003
		0.0025-0.005 mg/kg IV	In combination with butorphanol, excellent analgesia and muscle relaxation, beware of narrow therapeutic index	Murphy, 2003
Diazepam	Sedative	0.02–0.035 mg/kg IV 0.01–0.025 mg/kg IV	For non–painful diagnostics In combination with butorphanol for mild to moderate painful procedures	Murphy, 2003 Murphy, 2003
Flumazenil	Reversal	0.066 mg/kg IM 1 mg/10–20 mg midazolam or diazepam IV	For tranquilization, lasts 60–90 minutes Reversal for midazolam or diazepam	Bossart, 2001 Murphy, 2003
		Equal volume as midazolam IM	Reversal for midazolam	Walsh and Bossart, 1999
		Equal volume as diazepam IM	Reversal for diazepam	Bossart, 2001
Isoflurane	Anesthetic	0.5–5%	Similar settings as in domestic animals	Walsh and Bossart, 1999
Lidocaine 2% Meperidine	Analgesic Sedative, analgesic	Local infusion to effect Up to 1 mg/kg IM	Local analgesia In combination with midazolam for more painful procedures or anesthetic induction	Walsh and Bossart, 1999
		0.5–1 mg/kg IM	Sedation/analgesia for minor surgical procedures	Bossart, 2001
Midazolam	Sedative	0.02–0.05 mg/kg IM 0.045 mg/kg IM	Mild to moderate sedation Sedation for 60–90 min, can also use in conjunction with meperidine for more painful procedures or anesthetic	Murphy, 2003 Walsh and Bossart, 1999
		0.08 mg/kg IM	induction Anesthetic induction, intubation	Walsh and Bossart, 1999
Naltrexone	Reversal	1–2 mg/1 mg butorphanol IV	Reversal for butorphanol	Murphy, 2003
Xylazine	Sedative	Equal volume dose IM 0.05–0.1 mg/kg IM	Reversal for meperidine Moderate sedation, beware of narrow therapeutic index	Murphy, 2003
Xylocaine 1%	Epidural anesthetic	Dose not noted,	Used in one case for vertebral fracture	Bossart, 2001
Yohimbine	Reversal	epidural 1 mg/5–10 mg xylazine IV 2–3 mg/1 mg detomidine IV	surgery Reversal for xylazine Reversal for detomidine	Murphy, 2003 Murphy, 2003

^aIM, intramuscular; IV, intravenous.

Spinal needles are also used to obtain IV access for drug and fluid administration in anesthetized adult manatees in the caudal tail vascular bundle. This site is accessed by elevating the tail to visualize its ventral aspect or placing the animal in lateral or dorsoventral recumbency. Calves that are easily restrained due to size or illness are catheterized awake in the caudal tail site with 20- or 21-g 3.75- to 5-cm (1.5- to 2-in.) needles. The brachial vascular bundle is difficult to catheterize due

to needle placement perpendicular to the arteriovenous plexus. It is accomplished with 18-g 5-cm (2-in.) needles in adults and 20-g 3.75-cm (1.5-in.) needles in juveniles (Murphy, 2003). Although the pectoral flippers can be catheterized either medially or laterally, contact between the body wall and a medially placed catheter may displace it. Perivascular leakage of drugs can occur, potentially resulting in local tissue inflammation or necrosis. To reduce the likelihood of catheter displacement,

venous access is best attempted after sedative administration, tracheal intubation, and/ or final patient positioning for a medical or surgical procedure.

PRE-ANESTHETIC PREPARATION

Similar to other mammals, sirenians are physically examined and their bloodwork evaluated prior to anesthesia to identify any health conditions that would pose risks. Florida manatees present to rescue and rehabilitation programs with a variety of injuries and illnesses secondary to both natural and human causes, as have been described in previous mortality studies (O'Shea et al., 1985; Ackerman et al., 1995; Walsh and Bossart, 1999; United States Fish and Wildlife Service, 2001; Bossart et al., 2004). Two of the more commonly seen naturally occurring conditions in Florida manatees are cold stress and brevetoxicosis. Traumatic injuries from crab trap, monofilament line entanglement, or boat strike are also common presentations to rescue and rehabilitation programs. Understanding the extent of illness or injury is critical to assessing the anesthetic risk to a manatee patient.

Prior to anesthesia, sirenians are ideally fasted for 24 hours to reduce the likelihood of regurgitation. However, these species have a slow gut transit time (4–7 days in the Florida manatee and 5–9 days in the Amazonian manatee), so complete emptying of the GIT in 24 hours does not occur (Gallivan and Best, 1986; Walsh and Bossart, 1999).

Respiratory rates are monitored prior to sedation and through the induction procedure. In sirenians respirations are counted over 5 minutes to determine a rate because they are usually less than or equal to one breath/minute. If a manatee in the water shows signs of depression or incoordination after sedatives are administered, it is removed prior to the usual 20 to 25 minutes before handling. In animals with pulmonary compromise, oxygen supplementation with a portable oxygen tank and Hudson demand valve is often provided during short sedative procedures or prior to administration of general anesthesia.

MONITORING CONSIDERATIONS

Manatees are closely monitored during sedation and anesthesia using standard techniques or modalities used in domestic animals (see Chapter 6). Anesthetic depth is determined by assessing blink response, jaw tone, and resistance to limb movement. Eye position is often difficult to assess owing to recession of the globe into the orbit during anesthesia.

Physiological variables of the Florida manatee are listed in Table 44.3. Heart rates are calculated by either listening to the heart with a stethoscope or observing the pulsation of the skin overlying the heart when animals are positioned in dorsoventral recumbency. Electrocardiography, either by esophageal probe or

Table 44.3. Physiological parameters for the Florida manatee (*Trichechus manatus latirostris*).

Parameter	Range
Respiratory rate	Variable, avg 2–4 breaths/5 min in water, 3–15 breaths/5 min out of water
Heart rate	40–60 beats/min (can be as low as 30 with diving)
Body temperature	35.5-36°Ca
Tidal volume	2.9% of body weight ^b
Lung volume	Approximately 5% of total body weight

From Scholander PF, Irving L. Experimental investigations on the respiration and diving of the Florida manatee. *J Cell Compar Physiol* 1941;17:169-19; Pabst DA, Rommel SA, McLellan WA. The functional morphology of marine mammals. In: Reynolds JE III, Rommel SA, eds. *Biology of Marine Mammals*. Washington, D.C.: Smithsonian Institution Press, 1999:15-72; Walsh MT, Bossart GD. Manatee medicine. In: Fowler ME, Miller RE, eds. *Zoo & Wild Animal Medicine, Current Therapy*, 4th ed. Philadelphia: W.B. Saunders, 1999:507-516; Murphy D. Sirenia. In: Fowler ME, Miller RE, eds. *Zoo and Wild Animal Medicine*, 5th ed. St. Louis: Elsevier Science, 2003:476-482.

^aOral temperatures. Note that body temperatures are dependent on environmental water temperatures as well as site of thermometer placement.

^bBased on Scholander and Irving's work. N = 2.

pad/needle placement of leads on skin, is used for assessment of cardiac rate and rhythm. If esophageal probes are inserted orally care is taken to prevent the probe inadvertently being advanced into the trachea instead of the esophagus. It may be prudent to verify placement with a bronchoscope. Placement of a pulse oximetry probe on the tongue is difficult because of the short, thick shape and reduced mobility of sirenian tongues and their firm attachment to the lower jaw (Yamasaki, Komatsu, and Kamiya, 1980; Levin and Pfeiffer, 2002). Pulse oximetry readings are occasionally collected from the nasal septum, buccal mucosa, or rostral gingival ridge of the lower jaw. Rectal reflectance pulse oximetry probes are placed in the nostril to obtain saturation readings. Gingival capillary refill time is generally less than or equal to 2 seconds in manatees.

Body temperature is measured with a rectal, oral, or nasal probe. Flexible rectal thermometers are difficult to place owing to high sphincter tone and the fibrous consistency of feces obstructing advancement into the colon. Rectal temperatures read lower than core temperatures for these reasons (Irvine, 1983). Nasal passage of flexible probes is relatively easy; however, inhalation can result in spurious results because of mixture with ambient air. Oral placement of thermometers alongside the caudal buccal mucosa appears to give fairly accurate results, but equipment damage from the molars or accidental advancement into the trachea must be avoided.

End-tidal carbon dioxide (ETCO₂) levels follow those of other mammals; yet no scientific study has been reported, to the authors' knowledge, to correlate results with arterial blood gases. Samples for blood gas analysis have been collected from manatees, but the arteriovenous

plexus in the pectoral flipper, makes interpretation difficult. Venous or mixed samples are still diagnostically valuable when the animal is used as its own control during the procedure.

INTUBATION AND ANESTHESIA

Occasionally manatees can be intubated under midazolam sedation alone, but others require anesthetic induction with an inhalant administered by mask prior to endotracheal tube passage. Mask administration is usually done with a modified 20-L (5-gal) clear plastic water jug with the bottom removed. The edges are padded for a tighter fit over the animal's head (Walsh and Bossart, 1999). A large mask allows adequate tidal volume exchange with less resistance to rapid inspiration. Even in sedated manatees, breath-holding during mask induction can occur. The manatee patient may require stimulation, such as rocking side to side, to facilitate additional respirations during mask induction. Animals inadequately sedated for intubation often respond to sound, open their eyes partially, or retract their head when stimulated.

For intubation, a manatee's trachea can be accessed, at least theoretically, from both the oral or nasal cavities. Initial attempts at oral intubation in manatees were historically unsuccessful. Given the poor visualization of the caudal pharynx and larynx owing to the curved angle of the tongue, the narrow width of the buccal cavity, and the long soft palate, nasal intubation is preferred. Nasogastric tubes can be passed blindly in manatees, but dependable tracheal intubation is best accomplished with rhinoscopic assistance. Wild sirenians commonly have mild to heavy loads of nasopharyngeal trematodes, and in some cases, heavy parasitic infestations cause severe rhinitis or tracheitis and complicate intubation (Beck and Forrester, 1988; Bossart, 2001). In Florida manatees, it is recommended to use cuffed elongated foal endotracheal tubes (8-14 mm internal diameter, based on the size of the animal), as well as a stylet to assist passage into the laryngeal opening (Walsh and Bossart, 1999; Murphy, 2003). Because of the short length of the manatee trachea, care is taken to avoid intubation of a single bronchus. Passage of a bronchoscope down the endotracheal tube will confirm proper placement of the tube cranial to the carina. The endotracheal tube is secured to the muzzle with white waterproof tape strips secured to white tape encircling the muzzle caudal to the oral disk (Figure 44.5). Periodic suctioning of endotracheal tubes is required to remove mucous that accumulates in the tube (Walsh and Bossart, 1999). Once intubated, sirenians are maintained with isoflurane levels similar to those used in domestic animals (Table 44.3).

Mechanically assisted ventilation is necessary with general anesthesia to maintain adequate gas exchange and oxygenation. For shorter sedative procedures without inhalation anesthesia, oxygen supplementation is accomplished with an oxygen demand valve. When



Figure 44.5. Endotracheal tube securing on muzzle of a Florida manatee (Trichechus manatus latirostris).

mechanically ventilating a manatee, some unique anatomical and physiological traits need be considered. Mechanical ventilation does not mimic the sirenian respiratory cycle of inspiration closely following expiration. Rather, it reverses the cycle with expiration closely following inspiration. Higher respiratory rates on mechanical ventilators shorten time of lung inflation in a breath-holding species and leads to hypoventilation and hypercapnia. In the authors' experience, a slow inspiratory flow rate improves oxygenation while decreasing carbon dioxide accumulation.

In manatees pulmonary resistance is increased from other organs when they are removed from the water. In dorsoventral recumbency, the ventilator must counter the weight and pressure of abdominal organs and ingesta on the lungs. In sternal recumbency, the ventilator must also provide enough pressure to inflate the lungs despite limited lateral mobility of the pachyostotic ribs and ventral pressure from abdominal organs. Pulmonary resistance is further increased by loss of lung function from concurrent respiratory disease (e.g., severe pyothorax, pneumothorax, or pulmonary fibrosis or adhesions secondary to thoracic trauma). In these cases it may be difficult to alleviate hypercapnia or hypoxemia owing to loss of functional tissue. In some cases, whether because of disease or patient positioning, the peak inspiratory pressure of the ventilator must be adjusted above 20 mmHg to achieve lung expansion, oxygenation, and carbon dioxide exchange. Close monitoring of physiological variables determines the most appropriate ventilatory settings. Ventilations are initially set at 6 breaths/minute (Murphy, 2003).

Following recovery from anesthesia manatees are not placed in water until they are appropriately responding to stimuli and breathing voluntarily. If possible, animals are placed in shallow water (less than or equal to 1 m) so they are able to surface to breathe by pushing off the pool floor with their pectoral flippers.

The unique anatomy, physiology, and aquatic environment of sirenians make sedation and anesthesia

challenging. Continued efforts to develop knowledge of sirenian anesthesia are important to advance conservation efforts and improve our ability to treat sick and injured animals.

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45

Elephants and Hyrax

William A. Horne and Michael R. Loomis

INTRODUCTION

Elephants belong to the order Proboscidae, family Elephantidae. There are two surviving genera: *Loxodonta*, the African elephant, and *Elephas*, the Asian elephant. The genus *Elephas* consists of a single species with three subspecies: *Elephas maximus indicus*, the Indian elephant; *Elephas maximus maximus*, the Sri Lankan elephant; and *Elephas maximus sumatranus*, the Sumatran elephant. A fourth subspecies, *Elephas maximus borneensis*, has recently been proposed based on genetic studies (Fernando et al., 2003).

The genus *Loxodonta* is generally considered to be divided into two species: *Loxodonta africana*, the savanna or bush elephant, and *Loxodonta cyclotis*, the forest elephant (Roca et al., 2001). A third species (or possibly a subspecies), the West African elephant, has been proposed based on recent genetic studies (Eggert, Rasner, and Woodruff, 2002). Table 45.1 gives geographic ranges, heights, and weights of the different elephant taxa.

As of January 2006, 533 Asian elephants and 343 African elephants were registered with the International Species Information System (ISIS). Recent estimates for numbers of free-ranging elephants are 400,000 to 500,000 African elephants (World Conservation Union, 2002 IUCN Database) and 35,000 to 50,000 Asian elephants (Focus, 2005). These numbers indicate that the captive elephant population has nearly doubled in the last 15 years, and that estimates of wild elephant populations have declined by 30% (compared with Kock, Morkel, and Kock, 1993). Both captive and free-ranging elephants require sedation and anesthesia for a variety of reasons (Table 45.2). In captivity, elephants are sedated or anesthetized predominantly for medical reasons (although operant conditioning has allowed many minor procedures to be performed without anesthesia or sedation). These reasons are numerous and include a range of activities from dental work on tusks to Caesarian section.

Captive elephants also require long-term analgesia. In the coming decade more than 50% of all captive elephants will be 40 years old or older; osteomyelitis in the bones of the feet has been a significant cause of morbidity, often leading to euthanasia, in elephants of this age group.

By far, however, the vast majority of anesthetic episodes occur in free-ranging populations. These episodes generally involve translocations, various types of research, disease surveillance, and tracking-collar deployment for monitoring movement and land use patterns (Figure 45.1). Occasionally, free-ranging elephants are anesthetized for medical procedures such as removing a snare from a foot.

GENERAL CONSIDERATIONS FOR ELEPHANT SEDATION AND ANESTHESIA

Herd and Reproductive Behavior

Social structure and reproductive behavior must be considered in planning for anesthetic procedures both in field and captive settings. Elephants are long-lived (up to 65 years in the wild, 50 years in captivity), highly social animals that live in matrilineal family groups. The family group is led by a matriarch, who is generally the oldest and tallest female in the group. The group (Figure 45.2, top) consists of the matriarch and her descendants, her sisters and their daughters and their offspring. Males are driven from the family group before reaching sexual maturity (12–15 years) and live alone or in small dynamic groups.

With age, females acquire social knowledge that benefits the entire group. For example, groups with older matriarchs have higher per capita reproductive success (McComb et al., 2001). Moreover, matriarchs retain geographical memories that define the home range and corridors of seasonal herd migration patterns. For this reason, herd matriarchs are often selected for deployment of radio/satellite tracking collars ("tagging"), which requires 30 to 60 minutes of field anesthesia. The

Table 45.1. Geographic distribution, height, and weight of officially recognized elephant taxa.

Taxonomic Designation	Common Name	Geographic Range	Weight (kg)	Height (m)
Elephas maximus indicus	Mainland or Indian elephant	Indian Subcontinent, Southeast Asia, Peninsular Malaysia	2,000-5,000	2.5-3.5
Elephas maximus maximus	Sri Lankan elephant	Island of Sri Lanka	2,000-5,500	2.5-3.5
Elephas maximus sumatranus	Sumatran elephant	Island of Sumatra, Indonesia	2,000-4,000	2.5-3.2
Loxodonta africana	Savanna or bush elephant	East and South Africa	4,000-7,000	3.0 - 4.0
Loxodonta cyclotis	Forest elephant	Central and West Africa	2,000-4,500	2-3

 $\textbf{Table 45.2.} \quad \text{Procedures requiring elephant sedation or an esthesia.}$

Procedure(s)	Drug Protocol	Reference
Captive Elephants Standing Sedation		
Transport (juveniles)	Xylazine and ketamine	Heard et al., 1988 ^a
Abscess treatment,	Azaperone with local anesthetics	Ramsay, 2000 ^a
venipuncture, TB		
testing, manual		
ejaculation		
Aggressive abscess debridement	Azaperone and butorphanol	Ramsay, 2000 ^a
Trailer loading, cow-calf	Xylazine	Ramsay, 2000a; Abou–Madi
separation	26.1.	et al., 2002 ^c
Tumor excision,	Medetomidine	Sarma et al., 2002 ^c
wound dressing,		
subconjunctival		
injection		
Captive Elephants: Recumbent		
Immobilization		
Radiographs/dental	Etorphine and halothane	Heard et al., 1988 ^a
(juveniles)		
Castration	Etorphine	Fowler and Hart, 1973 ^c
Electroejaculation	Etorphine	Hattingh et al., 1994 ^a
Fractured tusk	Etorphine	Allen et al., 1984 ^a
management/repair	Etorphine and halothane	Tamas and Geiser, 1983 ^a ;
	Etorphine and isoflurane	Stegman, 1999a
Sole abscess	Valaria and lateralia	Dunlop et al., 1994 ^a
Sole abscess	Xylazine and ketamine followed by etorphine	Ollivet–Courtois et al., 2003 ^c
	and acepromazine	2003
Removal of infected phalanges	Etorphine and isoflurane	Gage et al., 1997 ^c
Umbilical herniorrhaphy	Xylazine, diazepam,	Abou–Madi et al., 2004 ^c
(juvenile)	ketamine and isoflurane	Abou-Madi et al., 2004
,	Returnine and isolitature	
Free-Ranging Elephants: Recumbent Immobilization		
Translocation	Etorphine and azaperone	Still et al., 1996 ^a
(juveniles)	Etorprinie una uzuperone	othir et al., 1990
Laparoscopic	Etorphine and azaperone	Stetter et al., 2005 ^a
reproductive	btorprimie una uzuperone	Stetter et al., 2000
sterilization		
Deployment of satellite	Etorphine	Kock et al., 1993 ^a ;
and/or radio tracking	r	Tchamba et al., 1995a;
collars		Ososfsky, 1997 ^a ; Elkan et al.,
		1998 ^b ; Horne et al., 2001 ^a
	Etorphine and	Elkan et al., 1998 ^b ;
	acepromazine	Dangolla et al., 2004 ^c
	Carfentanil	Elkan et al., 1998 ^b

Species of elephant sedated or anesthetized in the selected references:

^aLoxodonta africana, the African savanna or bush elephant.

 $^{^{\}mathrm{b}}Loxodonta~cyclotis,$ the African forest elephant.

^cElephas maximus, the Asian elephant.



Figure 45.1. Adult free-ranging female African elephant with satellite tracking collar deployed. The transmitter can be seen dorsally between the ears. The photograph was taken three minutes after intravenous injection of the etorphine reversal agent, naltrexone.

ecological success of the herd is thus very dependent on the successful outcome of the anesthetic procedure. As a result, the authors are strong advocates of providing 100% oxygen, intermittent positive pressure ventilation, and cardiopulmonary monitoring (discussed later), even in very remote locations.

Females reach sexual maturity at approximately 10 years; gestation lasts 22 months. Calves are weaned at 2 to 3 years, and the calving interval is 4 to 6 years. Over her lifetime, a cow may produce seven offspring; in the field, it is not unusual to observe a cow with an infant and two older offspring. The presence of multiple offspring can complicate anesthetic procedures enormously (Figure 45.2, *middle*). Although the oldest siblings typically follow the herd and separate from an anesthetized female when provoked by gunfire, the younger ones often do not (Figure 45.2, *bottom*). Infants weighing 100 to 200 pounds can often be managed by physical restraint; older, more aggressive offspring may require anesthesia to protect team personnel.

Physical Restraint

Free-ranging wild elephants must be adequately anesthetized in order to ensure the safety of all those involved in an anesthetic procedure. Physical restraint is impractical and dangerous. However, elephants in captivity can be trained to accept some forms of handling. There are two distinct handling approaches currently in use: free contact and protected contact. The former involves direct contact between the keeper and the







Figure 45.2. Free-ranging African elephants (Loxodonta africana) are highly social animals that live in matrilineal family groups. (Top panel) A small family group of adult females and their offspring. The activity of cattle egrets around herds is especially helpful in spotting elephants from a distance. (Middle panel) A single adult female may stray away from the herd and bring a number of offspring with her. (Bottom panel) Very young offspring are difficult to separate from their anesthetized mothers. Note the dart in the left hindquarter of the adult female. In this case, it was possible to physically restrain the infant while procedures were performed.

elephant, and often includes the use of an ankus to control the elephant. The legs are often chained for control (Fowler, 1995). Negative reinforcement is sometimes employed. The elephant is essentially placed in a subservient position to the keeper.

Free contact is potentially more dangerous than protected contact for the handler. Many zoological institutions feel that protected contact is a more preferable way to manage captive elephants. Here, the keeper is separated from the elephant by a protective barrier, often with access ports to access various body parts, especially

the feet or ears. The elephant, through operant conditioning, is taught to present body parts for inspection for minor procedures such as foot trimming or venipuncture. The elephant is positively rewarded for performing the desired behavior, and can choose whether or not to perform the behavior (Desmond and Laule, 1991).

In either approach, an elephant restraint device (ERD) may be used as an adjunct to restraint to perform more invasive procedures, such as reproductive evaluations (Figure 45.3). An ERD should allow safe access to all four feet, trunk, tusks, ears, face, both sides, hindquarters, and back by moving parts of the ERD or the elephant (Schmidt, 2003). Most ERDs are hydraulically operated and are large enough for an elephant to stand in comfortably for the duration of the procedure. The ERD should be constructed so that it can be quickly and easily opened in case an elephant falls down in the device.

Allometric Scaling

The energy cost of living (kJ/day) varies over a range of five orders of magnitude across species (Nagy, Girard, and Brown, 1999). Although there is no consensus as to whether energy cost scales as the 2/3 (surface area) or 3/4 (volume) power of mass, it is widely accepted that the physiological processes that underlie metabolic scaling are the same as those that regulate uptake, distribution, and elimination of drugs. Given that the elephant is the largest of all land mammals, it is important to consider allometric scaling when calculating dosages of drugs used for anesthetic procedures. When the energy cost (kJ/day) of a variety of mammalian species is plotted against the log of their individual masses (kg), the graph that results is a straight line with a slope of approximately 0.75. This indicates that metabolic rate (MR) varies according to the following simple relationship, $MR \propto (Mass)^{0.75}$. This fits with the general observation



Figure 45.3. Captive elephants can be trained to stand in an elephant restraint device for minimally invasive procedures.

that smaller mammals have higher metabolic rates than larger ones. Accordingly, this relationship can be used to extrapolate drug dosages to be used in elephants from known dosage regimens worked out for other placental mammals. [The relationship can also be applied across energy groups by introducing a taxa specific allometric constant (MR \propto K(Mass)^{0.75}] (Sedgwick, 1993).

The species most commonly used for comparison to elephants is the horse (Mikota and Plumb, Elephant Formulary, available at http://www.elephantcare.org/drugdex.htm). Assume, for example, that we want to give an average-sized African elephant (weighing 3000 kg) atropine as a pre-anesthetic agent. Although not used often in the horse, a published dosage for a 500-kg animal is approximately 0.05 mg/kg (Plumb VDH). To adjust the elephant's dose by taking the different metabolic rate into account, the following relationship applies:

(horse dosage) (horse metabolic rate)

- = (elephant dosage) (elephant metabolic rate), or $(0.05 \text{ mg/kg}) (500 \text{ kg}^{0.75})$
 - = (elephant dosage) (3,000 kg^{0.75})

Rearranging to solve for elephant dosage and solving for body mass raised to the 0.75 power,

elephant dosage =
$$(0.05 \text{ mg/kg}) (106)/(405)$$

= $(0.05)(0.26) = 0.013$

We see that the elephant dosage should be reduced by 74%. If this is a 6,000-kg male elephant, a 84% reduction would be required (substitute $6,000^{0.75}$ = 682 into the equation above). Thus, giving the published horse dose would result in a dramatic overdose. This may explain why a 28-year-old Asian elephant developed immediate central nervous system signs (central excitation leading to restlessness, irritability, disorientation, and ataxia) of atropine toxicity after receiving 0.05 mg/kg atropine IV (Gross, Clifford, and Hardy, 1994). The process of scaling down dosages has been applied to a variety drugs used in elephant sedation and anesthesia.

Tracheal Anatomy and Intubation

To maximize the safety of any anesthetic procedure in any species, it is very important to have access to, and control of, the patient's airway. This is especially true in the case of elephants, as etorphine, the drug used most commonly for induction and maintenance of anesthesia/immobilization, is a very potent respiratory depressant. In addition, as the animal goes down in either sternal or lateral recumbency, there is significant pressure on the diaphragm from abdominal contents. The combination of these two factors can result in severe hypoxemia and hypercapnia. Even though 70% of inhaled air is taken through the elephant's trunk,

attempts of positive pressure ventilation through the nares would prove futile as most of the forced air or oxygen would escape through the mouth. Complete control of the elephant's airway requires endotracheal intubation. Elephants are relatively easy to intubate; however, success of intubation requires an understanding of the unique feature of the elephant's larynx (Figure 45.4).

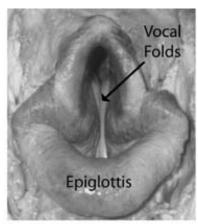
Intubation is done blindly, with the greatest success coming with hand-guided insertion of the tip of the endotracheal tube into the dorsal opening of the glottis. It is imperative that the mouth be opened wide enough to allow insertion of the arm, as elephants have large molars and a very narrow intermandibular space. The *top panel* of Figure 45.4 shows the larynx as it would be palpated when approaching from the oral cavity.

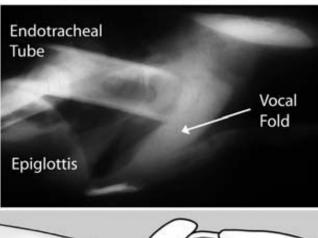
Elephants have a very large, fleshy epiglottis that is free of cartilage. It allows for a very tight seal to be formed between the trachea and the openings to the nares on the roof of the pharyngeal cavity. [The trunk and pleural adhesions that are unique to elephants are thought to have evolved for snorkeling] (West, 2002). The epiglottis is very pliable and can readily be pulled forward to allow access to the glottis. Elephants have very thick vocal folds that, at rest, largely occlude the entrance to the trachea. Difficulty in intubation, as shown radiographically in the middle panel of Figure 45.4, arises in part as the result of the curvature of the endotracheal tube causing its end to press up against the vocal folds. The solution to this problem is to, in coordination with breathing, manually guide the end of the tracheal tube to the dorsal aspect of the glottis where the vocal folds are much thinner and therefore more easily separated (Figure 45.4, lower panel).

Physiology

Allometric scaling predicts that a 3,000-kg elephant standing at rest would have a heart rate of 33 beats/minute (bpm) ($241 \times M^{-0.25}$), respiratory rate of 7 breaths/minute ($53.5 \times M^{-0.26}$), and tidal volume of 20 L ($6.2 \times M^{1.01}$). Although there are few references to substantiate these predictions in awake elephants, the numbers are in close agreement with what has been compiled to date (Mikota, 2003): heart rate, 25 to 30 bpm, and respiratory rate, 4 to 6 breaths/minute. Interestingly, the heart rate more than doubles in awake elephants lying in lateral recumbency (Honeyman, Pettifer, and Dyson, 1992). These physiological variables differ somewhat in anesthetized animals, as discussed in later sections.

Elephants have an average rectal temperature of 36° C to 37° C. Their packed cell volumes are comparable to other mammals (40%-45%); however, elephant red blood cells are large (MCV = 130 fl versus 50 fl for horses) and fewer in number compared with other mammals ($3-4\times10^6/\mu$ l versus $8-12\ 10^6/\mu$ l). Overall the oxygen carrying capacity of elephant blood is comparable to other





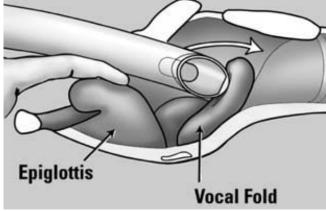


Figure 45.4. Anatomy of the elephant larynx. (Top Panel) Elephants have a large fleshy epiglottis and extremely thick vocal folds. (Middle Panel) The thickness of the elephant's vocal fold can be appreciated in this lateral radiograph of a dissected larynx. The curvature of the endotracheal tube makes intubation difficult. It is hard to get the end of the tube past the vocal folds. (Bottom Panel) Intubation can be achieved by manually guiding the end of the tracheal tube to the dorsal aspect of the glottis.

mammals (20–21 ml $\rm O_2/100$ ml). However, elephant hemoglobin binds oxygen with somewhat higher affinity than other species [$\rm P_{50}=23$ –24 mmHg versus 23–27 mmHg for the horse, and 29–31 mmHg for the dog (Dhindsa, Sedgwick, and Mecalfe, 1972; Cambier et al., 2004, 2005)].

It is also of interest to point out some physiological variables important to anesthesia that do not scale allometrically. These include mean arterial blood pressure (about 100 mmHg in all species), maximum functional capillary diameter, and fractional airway dead space (constant at about 25%–30% in large species). Plasma protein concentrations vary little with size or species.

Cardiopulmonary Monitoring in Remote Locations

Regardless of procedure location, it is very important to continuously monitor the oxygenation and ventilation status, blood pressure, heart rate and rhythm, respiratory rate, and temperature of anesthetized elephants. Monitoring anesthetized animals in remote geographic locations with no electrical power can be accomplished with the use of commercially available equipment or with modifications of available equipment. Portable solar panels that recharge batteries can ensure adequate power to operate most equipment. Equipment for monitoring oxygenation, ventilation, cardiac rhythm and rate, blood pressure, and core temperature have been successfully used in areas without an electrical grid or electrical generators (Figure 45.5).

Size, weight, power requirements, durability, and dependability in harsh environmental conditions should be considered when choosing monitoring equip-



Figure 45.5. Cardiopulmonary monitoring in remote locations. A portable solar panel (**A**) is used to recharge batteries. Adequacy of oxygenation and ventilation can be assessed with a portable pulse oximeter (**B**), blood gas analyzer (**C**), and capnograph (**D**). Adequacy of cardiovascular function can be assessed with a battery-operated ECG monitor (**E**), and a blood pressure monitor (**F**) than can be charged directly from the solar panel through a voltage regulator (**G**).

ment for field use. Of concern are power requirements and the source of the power, particularly in areas where there is no power grid or generator available. There are a number of types of rechargeable batteries on the market (http://www.nlectc.org/txtfiles/batteryguide/ba-type. htm, March 2004).

We use nickel metal hydride batteries (NiMH) in monitoring equipment in our studies (MAHA Powerx 2100mAh, Thomas Distributing, Paris, IL). NiMH batteries have several features that make them attractive for remote use. They can be recharged 500 to 1,000 times, have no memory, have a fairly steady discharge curve, and have a minimal negative environmental impact when disposed of. One disadvantage of NiMH batteries is that they have a self-discharge rate of 2% to 3% per day when not in use. AA-size NiMH batteries produce 1.2 V. Battery energy output is measured in milli-amp hours (mAh), with higher mAh ratings implying greater battery output. A battery rated at 1,700 mAh will produce 1,700 mA for 1 hour. Different manufacturers produce batteries with different power outputs. AA-size NiMH batteries are rated at up to 2,400 mAh.

Batteries are charged using fast, smart chargers attached to portable solar panels (iPowerUS fast smart charger, iPower, Arcadia, CA). A fast charger delivers the amount of current necessary to recharge the battery in 1 hour or less. In general, however, a slower charge rate will extend the overall life of the battery. To overcome the deleterious effects of rapidly charging a battery, a smart charger has a current-limiter built into it that reduces the current as the battery is charged, thereby limiting deterioration. The fast smart charger is attached to a portable solar panel (Sun Catcher Expedition solar charger, PowerQwest, Duluth, GA) via a 12-V "cigarette lighter" type plug. The panel (Figure 45.5A) produces 25 watts of power, which is more than enough power to charge 8 AA-size NiMH batteries at a time. Monitoring equipment that uses AA- or AAA-size batteries is preferred so that a large number of different-sized rechargeable batteries are not required in the field.

There are a number of commercially available cardiopulmonary monitors that can be adapted for use in the field. Oxygenation status is assessed continuously with a pulse oximeter and intermittently by arterial blood gas determination using a portable clinical analyzer. Several brands of pulse-oximeters have been successfully used and recharged in the field. An Invacare model 3402NV (Sims BCI, Waukesha, WI) is relatively small, lightweight, and operates on 6 AA-size batteries (Figure 45.5B). This pulse oximeter is durable and operates well on rechargeable AA-size NiMH batteries. An I-Stat portable clinical analyzer (Heska Corp., Fribourg, Switzerland) has been successfully used in the field using rechargeable 9-V NiMH batteries (Figure 45.5C). A challenge of using the I-Stat in the field is the analyzer's normal operating temperature of 16°C to 30°C (61°-86°F), which is often exceeded in typical elephant habitat. The I-Stat can be maintained at the proper operating temperature range by placing it in a 12-V thermoelectric cooler (Coleman, Spirit Lake, IA). The thermoelectric cooler can be powered directly off the solar panel.

Ventilation status is measured continuously by capnography (end-tidal CO_2 measurement) and intermittently by arterial blood gas determination. The criteria for choosing a capnograph include availability of a waveform display, mainstream and side-stream capabilities and power requirements. The Novametrix Tidal Wave model 615 (Novametrix Medical Systems, Wallingford, CT) meets these criteria (Figure 45.5D). The Tidal Wave comes standard with a rechargeable computer-type battery, but can be ordered with a battery tray which holds 7 AA-size batteries. This instrument is durable and operates well on rechargeable batteries. The side-stream capability allows a large-gauge needle to be placed in the lumen of a large endotracheal tube or respirator for sampling.

Cardiac rate and rhythm are monitored by use of an electrocardiograph (ECG). A compact ECG unit (Heska), which operates on 3 AAA-size rechargeable NiMH batteries, is durable and dependable in the field (Figure 45.5E).

Blood pressure can be measured using a direct arterial line or by indirect methods. Of the indirect methods, automated oscillotonometry has been successfully used in the field. We have not identified an automated blood pressure machine that runs on replaceable batteries. We have, however, modified a compact, durable instrument, Oscillomate 9300 (CAS Medical Systems, Branford, CT) for field use (Figure 45.5F). We manufactured a voltage regulator (Figure 45.5G), which is inserted between the internal battery of the blood pressure monitor and the solar panel. This allows the internal battery of the blood pressure monitor to be recharged directly from the solar panel.

All monitoring equipment, battery chargers and rechargeable NiMH batteries can be transported into the field in a backpack that is designed for photographic equipment (Lowepro Supertrecker AW II, Lowepro USA, Santa Rosa, CA). All of the above equipment has been dependably used to monitor immobilized elephants in a variety of remote habitats in Cameroon, including forest-savannah (hot and dry) and rainforest (hot and humid) locations.

IMMOBILIZATION OF FREE-RANGING ELEPHANTS

Etorphine

Etorphine is a non-selective opiate agonist that binds to μ , κ , and δ opiate receptors; consistent with the ability of the drug to activate G proteins, its effects occur at very low fractional receptor occupancy (Perry et al., 1982). Etorphine has been used safely for elephant restraint and anesthesia for nearly 40 years (Wallach and Anderson, 1968). The first in-depth report of the use of

etorphine for prolonged maintenance of an elephant in lateral recumbency for a surgical procedure was published by Fowler and Hart in 1973. Etorphine was used as the sole anesthetic agent on two separate occasions for castration of a subadult Asian elephant. Several important guiding anesthetic principles emerged from this report. First, it demonstrates that, by using incremental dosing or constant rate infusion of etorphine, elephants can be maintained in lateral recumbency for up to 3 hours and 40 minutes without adverse effects. Of particular importance is the fact that, even in the absence of fluid administration, the elephant under study did not develop post-anesthetic myopathy or nerve paralysis, conditions that are common in other large mammals subjected to prolonged recumbency.

Second, the report shows that it is possible to maintain adequate ventilation and oxygenation throughout the procedure. The authors went to great lengths to maintain a patent airway, provide a supplemental source of 100% oxygen, and maintain a surgical plane of anesthesia that did not compromise ventilation. Most importantly, they monitored for adequacy of oxygenation and ventilation by performing serial blood gas analysis.

Third, reversal of etorphine with diprenorphine was rapid and complete regardless of procedure time. The elephant stood within eight minutes following each procedure and was immediately able to eat, drink, and urinate. The option of immediate reversal added considerably to the safety of the anesthetic procedure.

A few other points from this report are worth noting. Given that the elephant was confined, the authors were able to induce anesthesia with a relatively low intramuscular (IM) dose (5-6 mg) of etorphine. Ataxia was noticeable within 6 minutes; an additional 5 to 10 minutes was required for the animal to lie down on its side. Maintenance of anesthesia for 1 hour required a total of approximately 10 mg of etorphine. As is a general property of opiates in all species, etorphine had minimal effects on cardiovascular function in this study. Neither anticholinergic agents nor sympathomimetics were required to maintain hemodynamic stability. Although blood pressure was not monitored, there was no evidence of hypotension (acidosis associated with poor perfusion, tachycardia) or hypertension (pulmonary hemorrhage). The elephant had minimal post-operative complications and was considered safe for elephant rides 5 months after surgery.

Lessons learned from this report have for the most part been carried into the field for larger-scale immobilization projects (Raath, 1993; Still, Raath, and Matzner, 1996; Osofsky, 1997; Horne, Tchamba, and Loomis, 2001). Larger initial doses of etorphine have been recommended for free-ranging elephants, often in combination with either acepromazine or azaperone. Carfentanil has been used instead of etorphine in some cases (Jacobsen et al., 1988); naltrexone has been used in the place of diprenorphine as a reversal agent.

Hyaluronidase has been used by some with the intent of improving uptake of the drug at IM injection sites.

Drug Delivery

Delivering anesthetic agents to free-ranging elephants can be very challenging. Terrain, equipment and infrastructure vary greatly across elephant range countries. Raath (1993) describes the use of helicopters or vehicles to approach elephants. In areas with limited infrastructure and no access to helicopters, approach on foot is necessary. Great care must be taken when approaching an elephant or a herd of elephants this way. An armed game guard and an experienced tracker should be part of the approach team. As elephants have excellent senses of smell and hearing, the approach should be from downwind and as quiet as possible. In areas in which there is access to cover, the approach should be from one area of cover to the next.

Perhaps most importantly, a long-range remote delivery system (RDS) should be used. (For a thorough review of RDSs, see Kreeger, Arnemo, and Raath, 2002.) Both CO₂ and powder-charge rifles are available, as are polyamide and aluminum syringes. Regardless of the RDS, 50- to 65-mm needles should be used to ensure an IM injection. The hind leg, back, and shoulder are preferred darting sites (Raath, 1993). If darting in the shoulder, care must be taken to avoid darting the ear. The dart impact should be perpendicular to the target site to ensure that the drug is delivered IM.

Elephants have relatively poor eyesight. The elephant will have limited ability to see the darter at distances greater than 40 feet. It is extremely important to know the position of all of the individuals in a herd so that the approach does not place the team within the perimeter of the herd. The shot should be taken from cover if possible. Although most elephants will run away from the darter, an elephant may occasionally charge the darter. Also, elephants may initially run in random directions after a herd mate is darted; this places the approach team in jeopardy. A human cannot outrun an elephant, but can run around a tree faster than an elephant can. It is a good practice to find a tree that an elephant can not easily push over, and not leave the tree until the charging elephant is at a safe distance. In forests, it may be necessary to dart an elephant from a distance of 10 meters or less because of the thickness of the surrounding vegetation. In such situations, it is extremely important to dart from behind cover. Once the elephant is darted, the tracker(s) should follow at a safe distance.

A "Typical" Etorphine Field Immobilization Procedure

All of our immobilization procedures have been initiated either from a vehicle (savannah regions) or on foot (forest-savannah or rainforest). What follows also applies to helicopter-assisted immobilizations, except

that physiological parameters measured in these elephants often reflect significant sympathetic stimulation. Adult, free-ranging female African elephants weighing 3,000 to 3,500 kg are typically administered a single IM 10- to 12-mg dose of etorphine delivered by dart to a region high on the hind limb. (Large males may require up to 20 mg.) At this dose, elephants show first effects in 3 to 5 minutes, but are capable of running at high speed over a long distance during this time. Within 10 to 15 minutes, the elephant often sits down into sternal recumbency. Although some elephants roll spontaneously into lateral recumbency, many remain in this sternal position. It is important to locate the elephant as soon as possible, as it is widely believed that elephants do not ventilate adequately while sternal. (Drug effects on breathing often cause the elephants to make a loud rumbling sound that can be heard over long distances.) While approaching the darted elephant, the remaining members of the herd, including offspring, must be frightened off with rifle fire.

An elephant found in sternal position must be rolled onto her side, which may require 6 to 10 people, depending on the size of the elephant and the terrain. While rolling the elephant, great care should be taken to protect the airway by extending the trunk. Heart rate, pulse pressure, respiratory rate, and arterial blood gases (blood drawn from auricular artery) should be evaluated immediately. Table 45.3 lists some of the published values for physiological parameters that have been recorded under similar field conditions. The elephant should have a very strong pulse as assessed by palpating an auricular artery. The table indicates that an etorphine immobilized adult female elephant, regardless of species, typically has a heart rate of 50 bpm and a respiratory rate of 5 to 7 breaths/minute. Any deviation from these values, whether higher or lower, should alert the anesthetist to the possibility of hypoxemia. This can be confirmed by arterial blood gas measurements. As is the case with most mammals, elephant hemoglobin begins to desaturate very quickly below an oxygen partial pressure of 60 mmHg ($SpO_2 = 93\%$).

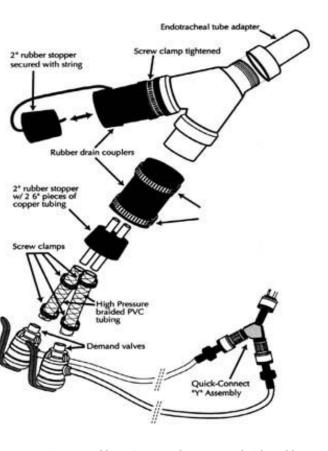
A number of elephant immobilization studies, including our own, have determined that etorphineimmobilized elephants are at-risk for developing severe hypoxemia ($PaO_2 = 40-60 \text{ mmHg}$). Although the actual number of hypoxemic elephants we have encountered is small (approximately 1 in 10), the importance of the matriarchal female to the social structure of the herd dictates that every effort be made to provide oxygen to immobilized elephants, even in remote locations. We have developed a simple and effective respirator device to provide oxygen and intermittent positive pressure ventilation to immobilized elephants in the field (Figure 45.6) (Horne, Tchamba, and Loomis, 2001). The respirator can be driven off a single MM oxygen cylinder (aluminum cylinders weigh 45 pounds) which holds 3,500 L of oxygen, enough for at least 45 minutes of

ble 45.3. Published cardiopulmonary values for etorphine-immobilized free-ranging elephants.

ecies (Sex)	HR beats/ min	MAP mmHg	RR breaths/ min	SpO ₂ %	PaO ₂ mmHg	EtCO ₂ mmHg	PaCO ₂ mmHg	Reference
orphine africana (ਰ A)	52ª		8					Wallach and Anderson, 1968
africana (♀A)	50		5					Kock et al., 1993
africana (♀A)	48 (34–80)			87 (70-96)				Osofsky, 1997
africana (♂♀J)	69 (56–112)		9 (3-28)	88 (82-95)	75 (50–99)		52 (38-70)	Still et al., 1996
africana (♀A)	50 (33–68)	105 (80–120)	7 (6–12)	95 (75–99) 95 ^c (93–97) ^c	63 (40–77) 251 ^c (97–491) ^c	47 (34–60) 47 ^c (33–50) ^c	60 (45–69) 58 ° (51–67)°	Horne et al., 2001
orphine and Acepromazine								
maximus (♂♀A)	52 (40-60)		7 (4–10)					Dangolla et al., 2004

^aAll single values are rounded averages.

^cFollowing 15 minutes of oxygen supplementation and intermittent positive pressure ventilation.



gure 45.6. A portable respirator can be constructed with readily ailable parts (for details see Horne et al., 2001). Oxygen is delivered rough two high-flow (160 L/minute) demand valves connected to an ygen cylinder (not shown).

continuous use. High partial pressures of oxygen (greater than 400 mmHg) can be achieved when the oxygen is delivered in synchrony with the elephant's breathing pattern through a 35-mm endotracheal tube with an inflatable cuff.

Placement of the endotracheal tube requires a team approach. The process is easy if the elephant has been properly dosed. Higher doses of etorphine tend to cause rigidity of the muscles of the jaw, making it difficult to access the pharyngeal cavity. With one person holding the tusk and pulling dorsally, and another pulling the lower jaw ventrally (a rope is helpful), the person inserting the tube lies on the ground and reaches between the jaws with the lower arm to locate the epiglottis. In large females, this is typically a full arm's length reach. Once the epiglottis is located (see Tracheal Anatomy and Intubation, above), the tube is passed alongside the arm and guided into the dorsal aspect of the glottis. The arm is removed, and the endotracheal tube cuff is inflated with a large syringe. The "Y" piece of the respirator is then connected by way of a standard endotracheal tube adapter, and oxygen is delivered through one side of the "Y" (inspiration port) by two demand valves connected in parallel. A large rubber stopper is used to plug the opposite side of the "Y" (expiration port) during inspiration and then removed during expiration. The respirator can deliver oxygen at a rate of 5 L/second; delivery over 4 to 5 seconds (elephant inspiration time) generates an adequate 20- to 25-L tidal volume with noticeable expansion of the chest wall.

^bValues in parenthesis indicate range.

Indirect methods of cardiopulmonary monitoring work well with immobilized elephants. Heart rate and SpO₂ can be monitored continuously via pulseoximetry with a large C-probe positioned on the tip of the tongue. End-tidal CO₂ can be monitored using a side-stream capnograph drawing from a needle inserted into the endotracheal tube (Figure 45.7). Blood pressure can be monitored oscillometrically with a small adult human cuff $(12 \times 30 \text{ cm})$ positioned at the base of the tail (Figure 45.8). As summarized in Table 45.3, three separate studies report SpO₂ values less than 93%, which is indicative of hypoxemia. Note also that endtidal CO2 values may under represent actual PaCO2 values by up to 25%, owing to the presence of physiologic dead space. Mean arterial pressures measure in the range of 80 to 120 mmHg, indicating that the 10-mg dose provides an adequate plane of anesthesia, at least for the placement of radio/satellite tracking collars.

Our experience has been that 10 to 12 mg of etorphine provides a full hour of immobilization without any signs of awakening; however, a typical collar deployment requires less than 45 minutes. We have not had to re-dose any cases in which it was clear that the drug delivery was complete with the first dart.

Pink Foam Syndrome

Opioids have been implicated as the cause of hypertension in elephants (Raath, 1993), with pulmonary hemorrhage being a common sequela. The pulmonary edema and bleeding is manifest as "pink foam" bubbling from the elephant's trunk. Surprisingly, we have not observed this effect of opioids in nearly 50 immobilizations. This is probably because the procedures we perform require that we approach elephants on foot, rather than by helicopter, as is common in South Africa in which pink foam syndrome has been reported. Approach on foot causes significantly less stress to the elephant. Secondly, the dose of etorphine that we use may be more appropriate for our procedures compared to previous reports of documented hypertension. Hattingh, Knox, and Raath (1994) reported mean arterial pressures greater than 185 mmHg in 5,000-kg bull elephants that had received only 8 mg etorphine; the pressure increased to greater than 260 mmHg during electroejaculation. The elephants were obviously not fully anesthetized. Azaperone and acepromazine have been recommended for use in elephants because of their vasodilatory effects, and because of their potential to reduce the probability of pulmonary hypertension. We have not found them to be necessary and believe that hypertension in elephants is not a direct result of opiate administration.

Recovery

Several drugs have proved to be effective in reversing opiates in elephants, including diprenorphine, nalmefene, and naltrexone. Because of the potential for renarcotization resulting from the reversal agent wearing



Figure 45.7. Continuous pulmonary monitoring using a pulse oximeter and capnograph while providing intermittent positive pressure ventilation. For pulse oximetry, a large C-probe is placed on the tip of the elephant's tongue. The sidestream capnograph draws expired air through a needle inserted into the expiration port of the respirator.



Figure 45.8. Blood pressure can be monitored continuously with a portable oscillotonometer and a small adult human cuff positioned near the base of the tail.

off too soon, we routinely reverse with naltrexone at 100 times the etorphine dose (1–1.2 g) given intravenously (IV). First signs of recovery—movement of the trunk and ears—generally occur within two minutes, and recovery is often complete within 10 minutes. Figure 45.9 shows the first stages of a typical recovery. Elephants roll into

sternal, throw their heads backward, and stand on their front legs first. They then stand on their hind legs, balance in a saw-horse position for a short time as the reversal becomes complete, and then amble off to find their herd mates. Given the promptness of recovery, it is

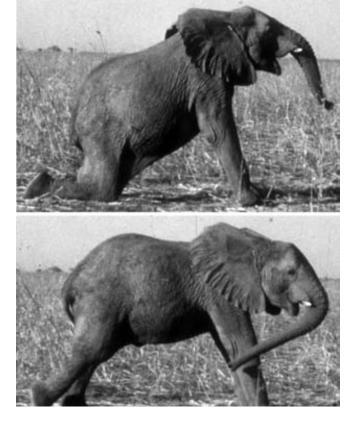


Figure 45.9. Recovery from etorphine anesthesia occurs within minutes following intravenous naltrexone administration. Elephants typically stand on their front legs first (Top Panel) and then adopt a saw-horse stance (Bottom Panel) until the drug has been completely reversed (several minutes).

Table 45.4. Drugs used for standing sedation in elephants.

essential that all equipment, vehicles, and personnel be a safe distance away prior to administration of the reversal agent.

CAPTIVE ELEPHANT PROCEDURES

Drug Delivery

Anesthetics and sedatives can be delivered to captive elephants by most acceptable means. Hand IM or IV injections can be given to conditioned elephants in captivity with or without the use of an ERD. For less tractable elephants, pole syringes or a variety of RDS may be required.

Standing Sedation

Standing sedation is useful in situations where a degree of sedation is required to perform a procedure that does not require general anesthesia. Procedures performed under sedation include treatment of abscesses, tuberculin testing, trunk washes for acid-fast culture, venipuncture, reproductive evaluations, manual stimulation of ejaculation, radiology, loading for transport, and transport (Ramsay, 2000). Sedation is often performed in conjunction with an ERD. Azaperone is preferred to α_2 -agonists for reproductive procedures (Schmitt, Bradford, and Hardy, 1996). However, there are anecdotal reports of azaperone causing excitement in elephants. Azaperone has been reported to cause paradoxical excitement in the horse (Dodam and Waterman, 1979). Xylazine/butorphanol provides a greater level of sedation than does azaperone (Ramsay, 2000). Xylazine can be reversed with the IM administration of yohimbine (0.5 mg per mg xylazine used), tolazoline (2 mg per mg of xylazine used) (Kock, Morkel, and Kock, 1993) or atipamezole (0.1 mg per mg xylazine used) (Kreeger, Arnemo, and Raath, 2002). Table 45.4 lists drugs and dosages commonly used for standing sedation of elephants.

Drug	Dosage mg/kg	Route	Species	Reference
Azaperone	0.08-0.09	IM	Loxodonta	Ramsay, 2000
Azaperone	0.017-0.046	IM	Elephas	Schmitt, 1996
Azaperone	0.060-0.150	IM	Loxodonta	Page, 1994
Azaperone	0.067	IM	Loxodonta	Raath, 1993
Haloperidol ^a	Variable with size of elephant	IM	Loxodonta	Raath, 1993
Butorphanol ^b	0.12	IM	Loxodonta	Ramsay, 2000
1	0.01-0.03	IV	Loxodonta	Ramsay, 2000
Xylazine ^c	0.2-0.3	IM	Loxodonta	Ramsay, 2000
Xylazine	0.080-0.150	IM	Elephas	Schmidt, 2003
Xylazine	0.110-0.550	IM	Loxodonta	Schmidt, 2003
Medetomidine	0.005	IM	Elephas	Sarma, 2002
Detomidine	0.0055	IM	Elephas	De Silva, 1994
Acepromazine ^d			*	Kock, 1993

^aUsed in conjunction with azaperone for transport of adult African elephants.

See reference for dosages.

^bUsed in conjunction with xylazine.

^cUsed in conjunction with butorphanol.

^dTotal doses of: 30 mg for an adult, 10–20 mg for a juvenile-adult and 5–10 mg for a baby-juvenile.

Table 45.5. Published cardiopulmonary values for etorphine-immobilized captive elephants.^a

Species (Sex)	HR beats/ min	MAP mmHg	RR breaths/ min	SpO ₂ %	PaO ₂ mmHg	EtCO ₂ mmHg	PaCO ₂ mmHg	Reference
Etorphine E. maximus (♂ A)	48 ^b (56-76) ^{c,d}		8		(74-93) (85-146) ^e		(44-49)	Fowler and Hart, 1973
L. africana	(44–100)		(7-20)		(67–73)		(29-78)	Heard
$(?, \delta J)$ L. africana $(?A)$		186 263 ^g			(80-516) ^f			et al., 1986 Hattingh et al., 1994
Xylazine, Ketamine,								
Etorphine E. maximus (&A)	(36-41)			(95-98)				Ollivet- Courtois et al., 2003
Etorphine and Halothane								
L. africana (PA)	(32-42)		(5-10)					Tamas and
L. africana (\mathcal{G} J)	50	106	10					Geiser, 1983 Heard et al., 1988
L. africana (\mathfrak{P} J)	61	106 ^h	(4-6)		$(140-277)^{i}$	(49-64)	(42-59)	Stegman, 1999
Carfentanil and Halothane								
E. maximus (♂A)	(47-60) ^j (110-125) ^d	(77-157) ^h	(4–12)		$(40-49)^{j}$ $(249-400)^{i}$		$(52-60)^{j}$ (52-78)	Dunlop et al., 1985
Etorphine and Isoflurane								
L. africana (♀A)	(60-90) ^j (50-70) ^d	$(120-240)^{j}$ (110-170)	$(6-8)^{j}$ (2-5)		(45-75) ^j (100-350) ⁱ	(20-35)	$(40-50)^{j}$ (45-68)	Dunlop et al., 1994
Xylazine, Ketamine and Isoflurane								
E. maximus (さ 2 mo old)	(55-60)		(10-30)	≥97	(152-558) ⁱ		(55-61)	Abou–Madi et al., 2004

^aA, adult; J, juvenile.

Etorphine Induction and General Anesthesia

A variety of anesthetic protocols have been used in captive elephants. A summary of published cardiopulmonary values obtained during these procedures are listed by protocol in Table 45.5. As mentioned, the striking difference between published free-ranging and captive elephant procedures is the method of administering etorphine as an induction agent. For example, rather than a single dose of 10 to 12 mg etorphine IM, Dunlop et al. (1994) have reported that, in two out of three attempts, 6 mg etorphine administered by pole syringe was sufficient to allow an elephant to be positioned into sternal recumbency. An additional 2 mg of etorphine administered IV permitted positioning in lateral

recumbency. In a third attempt, the elephant appeared to be apprehensive and stressed and required an additional 7 mg of etorphine and a 210-mg dose of azaperone.

Maintenance of a surgical plane of anesthesia for prolonged periods can be achieved by repeated 1- to 2-mg doses of etorphine (Fowler and Hart, 1973; Allen et al., 1984) or with inhalation anesthetics (Tamas and Geiser, 1983; Heard et al., 1988; Dunlop et al., 1994; Stegmann, 1999). Inhalation anesthetics have also been used following induction with carfentanil (Jacobsen et al., 1988) and xylazine-ketamine (Abou-Madi et al., 2004). As with any species, recoveries from inhalation anesthetic procedures may be prolonged. Opiates should be reversed, even if it has been several hours since they were administered.

^bAll single values are rounded averages.

^cValues in parenthesis indicate range.

dIntraoperative range.

eWith 100% oxygen insufflation through the trunk.

^fWith 100% oxygen delivery through Hudson demand valve.

^gDuring electroejaculation.

^hCalculated [0.3 (average systolic pressure-average diastolic pressure)].

ⁱWith 100% oxygen delivery through a semi-closed anesthetic circuit.

^jValues with opiate alone.

ANALGESIA

Nonsteroidal Anti-inflammatory Agents

Although nonsteroidal anti-inflammatory agents (NSAIDs) are used extensively in elephants, very little pharmacokinetic data are available. Ketoprofen was studied by Hunter, Isaza, and Koch (2002). Dosage recommendations resulting from their study are 1 to 2 mg/kg every 24 to 48 hours, IV or PO. Table 45.6 lists NSAIDs commonly used in elephants. Care should be used in treating elephants with other NSAIDs. Extrapolation of elephant dosages from equine pharmacokinetic parameters is inappropriate (Hunter, Isaza, and Koch, 2002). Metabolic scaling dosages and treatment intervals for elephants may correlate with pharmacokinetic data (Mortenson, 2001; Hunter, Isaza, and Koch, 2002).

SUMMARY

Despite their very large size, elephants can be readily anesthetized and stably maintained for hours under both free-ranging and captive conditions. Fortunately, they respond very predictably to the potent opiate agonists etorphine and carfentanil. Whether the opiates are used alone or in combination with inhalation anesthetics, it is possible to maintain hemodynamic and respiratory stability for many hours without pharmacological intervention. Quite amazingly, a number of multiple-hour anesthetic procedures have been performed without any post-anesthetic complications, such as nerve paralysis or myopathy.

As with any anesthetic procedure, it is important to monitor cardiopulmonary function and temperature continuously in elephants. Monitors developed for companion animal species are readily adapted to the elephant, even in remote locations. Of all the potential complications that might be expected during anesthesia, elephants are most at risk of developing hypoxemia.

Table 45.6. Commonly used nonsteroidal anti-inflammatory agents used in elephants.^a

Drug	Dose mg/kg	Method of Determination	Reference
Flunixin	1.0 every 24 hours	Empirical	Mortenson, 2001
Flunixin	0.7 every 40 hours	Metabolic scaling ^b	Mortenson, 2001
Ibuprofen	0.5–4.0 every 24 hours	Empirical	Mortenson, 2001
Phenyl- butazone	1.0-2.0 every 24 hours	Empirical	Mortenson, 2001
Phenyl- butazone	4.0 every 12 hours	Metabolic scaling ^b	Mortenson, 2001
Ketoprofen	1.0-2.0 every 24-48 hours PO or IV	Pharmacokinetics	Hunter et al., 2003

^aEmpirical doses may not be appropriate.

We and others have shown, however, that hypoxemia is readily corrected by simple oxygen supplementation. We recommend that, whether by continuous insufflation or intermittent positive pressure ventilation, some means of oxygen supplementation be readily available for use when anesthetizing elephants. This is especially true in field situations, in which severe hypoxemia is most likely to occur.

HYRACOIDEA

The hyraxes have traditionally been classified closely to the *Proboscidea* or elephants. The family Procaviidae is made of three genera, including the *Procavia* and *Heterohyrax*, which are primarily terrestrial species. The third genus is the *Dendrohyrax* or tree hyraxes, which are primarily arboreal.

The *Procavia* or rock hyrax is the most common species found in zoological institutions. This species has been implicated as a reservoir host for cutaneous leishmaniasis, an important zoonotic disease (Svobodova et al., 2006). Also, rock hyraxes in zoos have been diagnosed with hepatic hemochromatosis and cardiomyopathy that could affect anesthetic management (Langan, personal communication). Rock hyraxes have continually growing upper incisors and a normal body weight of 3 to 4 kg. Venous access sites include the jugular or femoral veins. An adult rock hyrax can accommodate an endotracheal tube of 4 to 5 mm in diameter, but can be very challenging to intubate.

Rock hyrax can become very stressed with physical restraint and capture. Ideally, they should be trained to go into a box or kennel that can be used for chamber anesthetic induction. In one study, peridomestic rock hyrax were baited with leaves to enter a raccoon trap (Svobodova et al., 2006). The animals were live trapped and then immobilized with ketamine IM at 10 mg/kg. Most zoo veterinarians prefer to anesthetize rock hyrax with inhalants such as sevoflurane or isoflurane delivered by face mask or in an induction chamber. Injectable anesthetic agents can also be used and include tiletamine/zolazepam at 2 to 4 mg/kg. Ketamine at 10 mg/kg with xylazine at 2 mg/kg can be given IM to immobilize rock hyraxes but this combination has a narrow range of safety when compared to inhalant anesthesia.

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bBased on a 3,200-kg elephant.

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46 Non-domestic Equids Chris Walzer

INTRODUCTION AND TAXONOMY

The equidae family encompasses the zebras, asses, and horses. These descended some 50 million years ago from the "dawn horse" (Hyracotherium) with the equus emerging in the Pleistocene, about 1.5 million years ago. The taxonomy of the non-domestic equidae is controversial; ISIS lists eight wild species with several subspecies: three zebras and one wild ass in Africa, and three wild asses and the Przewalski's horse in Asia (Table 46.1). They are distributed solely throughout the Old World, from the deserts of Namibia across the plains of eastern Africa to the high altitude semi deserts of central Asia. In addition to the wild equidae feral horses and donkeys (or burros) exist on all continents except Antarctica. Generally the present-day equids exploit the semiarid grasslands, where they play a key role in the functioning of natural grazing systems. Within their natural range many equids are subjected to extreme weather conditions. For example, temperatures range from -45°C in the winter to 40°C in the summer with diurnal temperature ranges in excess of 35°C at the reintroduction site for Przewalski's horses in the Dzungarian Gobi in Mongolia. The equidae use a great range of altitudes within their present-day distribution, 60-m b.s.l. (Danakil: Somali wildass) and 5000 m a.s.l. (Tibet: Kiang) (Strauss, 1995). For further information concerning the status and geographical distribution of the various subspecies the reader is referred to the IUCN/SSC Equid specialist group publications (Moehlman, 2002). Of particular importance in the captive and medical management of the wild equids is an understanding of their two distinct social systems (Moehlman, 2002). In the equids of the arid habitats, some males defend territories, preferably near water sources, which confers mating rights over females when they enter the territory. Asses and Grevy's zebra form loose groups and the only long-term relationships occur between mother and offspring for a period of 2 years. Asses in central Asia may aggregate to loose groups in excess of several hundred

individuals. The other equid species form permanent family groups, so-called harem groups. In this system, life-long relationships between adult individuals are formed. Young males form bachelor groups. The various social systems must be considered when managing these species in general, but especially the removal of individual animals from a harem group during anesthesia must be critically evaluated.

ANATOMY AND PHYSIOLOGY

The anatomy and physiology of the wild equids is similar to that of their domesticated counterparts (Table 46.2). The mountain zebras (E. z. hartmannae and E. z. zebra) are distinguished from other zebra species by a "gridiron" pattern formed by stripes on the rump and a small dewlap on the throat (Duncan, 1992). The Grevy's zebra (*E. grevyi*) is the largest wild equid. They are easily recognizable on the one hand because of their size, and on the other because of the large ears and distinct fine stripe pattern. The plains zebras (E. burchelli spp.) are one of the most abundant ungulate species in Africa. Subspecies can be distinguished by the variations in their stripe patterns. The classification and number of the subspecies is controversial. The African wild asses are sympatric throughout their range with the domestic African donkeys and it is probable that the genomes of the wild and domestic asses are extensively mixed. Unlike the Przewalski's horse and domestic horse, the wild asses and donkeys have the same number of chromosomes and appear similar. Differences persist in leg colors, counter shading, and shoulder crosses. The Asian wild asses (E. onager, E. kiang, E. hemionus) vary little in size, but skeletal and color differences allow the various subspecies to be distinguished. The Prezwalski's horse (E. c. prezwalskii) is closely related to the domestic horse; although they are distinct in the number of chromosomes (Prezwalski's horse 2n = 66; Domestic horse 2n =64) their hybrids are fertile (Ryder, Epel, and Bernischke, 1978). The Prezwalski's horse has an erect mane, and the

proximal aspect of the tail has short guard hairs. Most Prezwalski's horses have a dark stripe along the back and distinct horizontal stripping of the palmar aspects of the front legs. Latest genetic research has shown that the Prezwalski's horse is most probably not the direct ancestor of the present domestic horses, but more likely a sister taxa (Wallner et al., 2003).

VASCULAR ACCESS SITES AND MONITORING

Vascular access is easily performed in the various equid species. As a routine measure an IV catheter should be placed during all equid anesthesia procedures, as this provides constant venous access if an emergency should arise or additional drugs must be provided. The jugular veins provide an excellent venous access site for standard over-the-needle catheters. Large-bore catheters

Table 46.1. Present-day wild equids based on ISIS (2006) taxonomic tree.

Genus	Species	Subspecies	Common Name
Equus	Asinus	Africanus	Nubian wild ass
		Somalicus	Somali wild ass
	Onager	Khur	Indian wild ass
		Kulan	Turkmenian wild
			ass/ Kulan
		Onager	Persian onager
	Kiang	Holdereri	Eastern kiang
		Kiang	Western kiang
		Polyodon	Southern kiang
	Hemionus	Hemionus	Mongolian wild ass
		Luteus	Gobi dziggetai
	Caballus	Przewalskii	Przewalski's wild
			horse
	Burchelli	Antiquorum	Damara zebra
		Boehmi	Grant's zebra
		Burchelli	Burchell's zebra
		Selousii	Selous' zebra
		Chapmanni	Chapmann zebra
	Grevyi	-	Grevy's zebra
	Zebra	Hartmannae	Hartmann's mountain Zebra
		zebra	Cape mountain zebra

should be used to provide adequate fluid flow rates. At least 14 standard wire gauge (swg) should be used (Taylor and Clarke, 2007). These can be placed either with or against the flow. Placing catheters against the flow (toward the head) is often easier and reduces the risk of air entrapment (Taylor and Clarke, 2007). Alternative venous access sites are the distal branches of the saphenous vein and the external thoracic vein. Arterial access and catheter placement is most easily achieved in the facial and transverse facial artery. These sites can be used to determine the pulse rate; collect arterial blood samples for blood gas analysis and direct blood pressure monitoring. The handling and storage of arterial blood samples may affect blood gas values (Klein et al., 2005).

In general, anesthesia monitoring in the wild equid species is analogous to the domestic horse. Anesthesia monitoring should be implemented as soon as the animal is fixed. Sequential rectal temperature measurements, thorax excursion to determine breaths per minute, and auscultation for heart rate are the absolute minimum in anesthesia monitoring. Relative percent oxyhemoglobin saturation measured with a batterypowered pulse oximeter (e.g., Nellcor NP-20, Nellcor Inc., Pleasanton, CA) is useful to determine arterial oxygenation and gives good insight into respiratory function. Pulse oximeter probes can be affixed to the tongue, nasal septum, and the plucked ear (Figure 46.1). Several excellent reviews have been published; the reader is referred to these (Saint John, 1992; Taylor and Clarke, 2007).

INTUBATION

Endotracheal intubation is easily achieved in the equid species. The head is extended for intubation. When using the almost straight silicone endotracheal tubes (ET), these can be advanced directly into the trachea. When using the older curved red-rubber type ET, the ET is initially advanced with the concave curve dorsally till the soft palate is dislodged from the epiglottis and then rotated 90 degrees and passed on down the trachea (Taylor and Clarke, 2007).

Table 46.2. Biological data of the wild equids.

	Birth Weight	Adult Weight	Life Expectancy	Reported Gestation Length	Nursing in Months
Prezwalski's horse	45	250-375	33	330-340	6-8
Asian wild ass	25-30	200-250	29	330-360	6-9
African wild ass	20-30	250-300	24	360	4-6
Grevy's zebra	20-30	350-450	35	387-428	6-13
Plains zebra	33	350-450	29	365-375	6-10

Adapted from Strauss G. Einhufer. In: Göltenboth R, Klös H-G, eds. *Krankheiten der Zoo- und Wildtiere*. Berlin: Blackwell Wissenschafts-Verlag, 1995:189–200; Duncan P, ed. *Zebras, Asses, and Horses: An Action Plan for the Conservation of Wild Equids*. Gland, Switzerland: IUCN, 1992.



Figure 46.1. Portable pulse oximeter probe affixed to the tongue of an Asiatic wild ass.

NON-CHEMICAL CAPTURE OF EQUIDS

Although physical restraint cannot be recommended for any wild equid except possibly newborn foals, nonchemical capture methods have been employed in the zoo-born Przewalski's horse. In the course of the various reintroduction projects to Mongolia, specific techniques and methods have been developed to facilitate loading. For the first time in 2002 non-chemical capture and crating was possible for the majority of the zooborn horses. The system was based on training each individual horse to feed in large crates over a period of several weeks. These crates are subsequently closed using a remote system and the horses moved into the smaller transport crates (Figure 46.2) (Walzer et al., 2004). In 2005 a similar simplified system was also used successfully in Takhin Tal, Mongolia, to move eight horses into the west of the Gobi B strictly protected area (Schönpflug and Walzer, unpublished data).

Individual transport crates for equids are based on the IATA recommendations but have been adapted over the years for this specific air freight transport scenario; however, are most probably beneficial for all equid transports (IATA, 2006). Head and neck movement in the crate has been limited in order to reduce the risk of a horse turning onto its back while inside the crate at take off during air transport (Figure 46.3). The headroom of the crates is additionally lined with high-density foam mats to limit abrasions and trauma caused by head rubbing. Alternatively and for land transport equids can be mass crated (Openshaw, 1993).

CHEMICAL RESTRAINT AND CAPTURE

Oral Sedation

Varying degrees of sedation can be achieved using acepromazine as granules (Vetranquil 1%, Albrecht, Germany) or as a paste (Sedalin, Chassot, Switzerland)

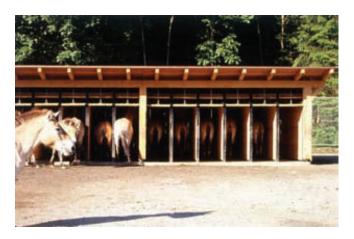


Figure 46.2. Non-chemical capture of the zoo-born horses. Individual horses are fed in large crates over a period of several weeks. These crates are subsequently closed using a cable controlled remote drop-door system.



Figure 46.3. Head and neck movement in transport crates is restricted with padding in order to reduce the risk of a horse turning onto its back at take off during air transport.

at a dosage of 0.5 to 1.5 mg/kg by mouth (PO). The granules are mixed into moistened pelleted feed, and alternatively the paste is placed in apples, both of which are then readily consumed by the animal. Although this is not sufficient for subsequent physical restraint it has proven valuable as a transport and pre-immobilization sedation (Wiesner, 1993).

Parenteral Sedation

Various drugs, especially α_2 -agonists and acepromazine (Vetranquil 1%), have been used to sedate wild equids. Detomidine (Domosedan, SmithKline Beecham Animal Health, West Chester, PA) at 20 to 80 µg/kg IM has been used successfully in some wild equids (Morris, 1992; Vitaud, 1993). In contrast to the experiences gained with detomidine these authors warn against using the α_2 -agonist medetomidine (Dormitor, SmithKline Beecham Animal Health) alone as a preanesthetic

because of the occurrence of significant ataxia (Morris, 1992). Similarly, romifidine (Sedivet, Boehringer, Germany) has been shown to cause ataxia (Wiesner and von Hegel, 1990). Acepromazine is used at a dosage of 0.15 to 0.25 mg/kg intramuscularly (IM). Furthermore, azaperone at a dosage of 200 mg has been suggested for the sedation of zebras (Burroughs, 1993b). Several other drugs would potentially be useful in sedating equids but are impracticable in their use because of the large volumes necessary.

Long-acting Neuroleptics

When long-term sedation is required, as during a transport process, this is best achieved using one of the longacting neuroleptics (LAN). This group of drugs can be used to reduce anxiety and stress during long-distance translocation, and for reintroduction into novel enclosures and habitats. As a result of the delayed absorption of the neuroleptics, it is prudent to combine a longacting tranquilizer with a short-acting analogue (Ebedes, 1992). Haloperidol belongs to the butyrophenone group of neuroleptics with a longer duration of activity. It is available in Europe as a 5 mg/ml injectable solution (Haldol) that can be applied IM and intravenously (IV). Furthermore, 1- and 10-mg tablet forms (Haldol) for oral application are also available. It is important to note that in Europe, haloperidol is also available as a decanoate ester (Haloperidol decanoate, Janssen-Cilag) an oily form that results in a long-term deposit. Haloperidol decanoate results in a prolonged sedation of up to 25 days and its effects are generally unsatisfactory because of adverse side effects such as inappetence and central nervous system (CNS) symptoms (Swan, 1993). Zuclopenthixol acetate is a thioxanthene similar to the phenothiazine group of tranquilizers. Through esterification with the acetate and dissolution in vegetable oil, absorption and duration has been extended. It is available as 50 mg/ml injectable solution (Ciatyl-Z-Accuphase, Bayer, Leverkusen, Germany). Similar to haloperidol, zuclopenthixol is also available in some countries as a decanoate ester, again the duration is extended, but once again the effect seems inadequate (Swan, 1993). Perphenazine is a phenothiazine derivative with a piperazine side chain. It is available as a 100 mg/ml injectable solution in the enanthate ester form, dissolved in sesame oil (Decentan

Depot, Merck KgaA, Darmstadt, Germany). When compared with haloperidol and zuclopenthixol, perphenazine has a markedly prolonged duration of action that can subsist for 10 days. These neuroleptics have been used successfully in various zebra species (Swan, 1993) and in the Przewalski's horse (Atkinson and Blumer, 1997; Walzer et al., 2000). Extrapyramidal symptoms (EPS) a neurological side effect, causes a variety of symptoms, such as involuntary movements, tremors, changes in breathing and heart rate, and inappetence have been recorded as the most important side effects of LAN. The EPS can be treated with biperidine (Akineton, Knoll, South Africa) and Diazepam (Valium, Roche, Switzerland). The use of long-acting neuroleptics has greatly facilitated the in-crate phase during flight (36 hours) and re-loading of Przewalski's horses. This author presently recommends treatment with a combination of 0.2 to 0.3 mg/kg haloperidol (Haldol, Janssen-Cilag) and 150 to 200 mg/adult equid perphenazine (Decentan-Depot). It is important to carry out this treatment at least 12 to 24 hours prior to transport or anticipated stress influence (Table 46.3).

Anesthesia

Applying drugs over a greater distance requires specific remote delivery systems. For an excellent review of the various available systems the reader is referred to Kreeger et al. (2002) and chapter 4 in this book. The author recommends the use of a CO₂-propelled dart guns such as the Daninject JM model (Daninject JM, Wildlife Pharmaceuticals, Fort Collins, CO). Previous authors have warned against using high velocity gun systems (e.g., Cap-Chur system) in zebras due to their thin skin (Burroughs, 1993a). When working in the wild this author prefers to use new 3-ml darts discharged by expanding compressed air (Daninject). Old darts are not used, as these are never as accurate. By shortening the dart stabilizers to 3 cm the effective range is 80 m under ideal conditions (Lengger, Walzer, and Silinski, 2002). However, this distance is significantly reduced in the windy conditions. A sufficiently long dart needle of 55 mm is required to efficiently dart an Asian wild equid in good condition during the late summer and fall, due to significant layers of fat in the rump region. For zebras a needle length of 25 to 30 mm has previously been recommended (Burroughs, 1993a). In captive zebras this is

Table 46.3. Suggested dosages for long-acting neuroleptics in selected wild equids.

Drug	Burchell's Zebra	Hartmann's Zebra	Przewalski's Horse	Onset of Sedation	Duration
Haloperidol	0.3 mg/kg	0.28–035 mg/kg	0.2–0.3 mg/kg	5–10 minutes	8–18 hours
Zuclopent-hixol	50–100 mg/adult	50–100 mg/adult	50–100 mg/adult	1 hour	3–4 days
Perphenazine	100–200 mg/adult	200 mg/adult	150–200 mg/adult	12–16 hours	10 days

Based on Swan GE. Drugs used for the immobilization, capture, and translocation of wild animals. In: McKenzie AA, ed. *The Capture and Care Manual*. Pretoria, South Africa: Wildlife Decision Support and the South African Veterinary Foundation, 1993: 2–64; Walzer C, Baumgartner R, Robert N, et al. Medical aspects in Przewalski horse (*Equus przewalskii*) reintroduction to the Dzungarian Gobi, Mongolia. *Proc Am Assoc Zoo Vet* 2000;7–21.

most probably too short and the use of 55 mm should be considered. The use of wire barbs or collars on the needle to securely retain the dart in the animal is recommended in order to enable complete drug expulsion. Once an animal is successfully darted one should attempt to keep it in sight. However, it is very important at this stage to not disturb the animal any further by chasing it or approaching before the drugs have taken full effect. Once the animal has become recumbent, an approach on foot from behind and immediate fixation of the head is recommended (Figure 46.4). Be aware that in the first few minutes of recumbency the animal may become aroused by voices or loud noises and attempt to rise and flee further. Anesthesia monitoring should be implemented as soon as the animal is fixed.

The agent of choice for wild equid immobilization and anesthesia is the potent opiate ethorphine. The opiates interact in the CNS with stereo-specific receptors (Kreeger et al., 2002). Various receptors have been identified. These are classified as κ , δ , σ , and μ receptors. A major advantage in the use of the opiates is the specific opiate antagonists that allow for the complete reversal of the anaesthetic effects. Whereas some agents can be classed as sole antagonists (e.g., naltrexone), others have agonist-antagonist properties (e.g., diphrenorphine). The opiate ethorphine is an analogue of thebaine and in humans is 500 times more potent than morphine (Jasinski et al., 1975; Kreeger et al., 2002). Ethorphine at 2.45 mg/ml is available in Europe and many other parts of the world in combination with acepromazine 10 mg/ml (Large Animal Immobilon, C-Vet Veterinary Products, Leyland, UK). Furthermore ethorphine is available as a mono substance at 4.9 and 9.8 mg/ml (M99, Vericore Ltd., Dundee, Scotland). All products are supplied in a container together with the antidote diprenorphine or M5050 in the respective ade-



Figure 46.4. The head of a horse should be fixated at all times during an immobilization procedure. The knee is best placed laterally on the maxilla.

quate dosages. The use of diprenorphine to antagonize ethorphine in non-domestic equids may increase the likelihood of renarcotizations. In North America, because of difficulty in obtaining ethorphine, a similar, more potent opiate, carfentanil (Wildlife Pharmaceuticals) has been used extensively in equids (Allen, 1992, 1994, 1997; Klein and Citino, 1995). However, the effects of carfentanil cannot be equated with those of ethorphine as the procedure is markedly rougher with significant muscle contractions (Morris, 1992). In the past years several additional non-narcotic immobilization protocols have been developed and used more or less successfully in wild equids (Morris, 1992; Vitaud, 1993; Matthews, 1995). For prolonged surgical procedures intubation and inhalation anesthesia with isoflurane or halothane is recommended.

For wild equid anesthesia, this author presently recommends a combination of the opiate ethorphine (M99, C-Vet Veterinary Products, Lancs, UK), the sedative α_2 -agonist detomidine (Domosedan) and the mixed antagonist-agonist opioid butorphanol (Torbugesic, Fort Dodge Animal Health, Orange City, IA). Detomidine acts on the α_2 -adrenergic receptors where it inhibits the release of norephinephrine. Butorphanol is a μ-opioid receptor antagonist that alleviates the marked respiratory depression induced by the ethorphine at the μ-receptor and potentiates the sedative effect at the κ and σ receptors. Furthermore this combination has significantly limited the ethorphine specific pacing, which greatly reduces the distance an equid travels after darting. This is particularly important in open steppe habitats where equids darted without the addition of butorphanol can cover several kilometers before becoming recumbent. However, the combination still allows for "walk-in" crate loading. Ethorphine is reversed with the opioid antagonist naltrexone at a rate of 20:1 (Trexonil, Wildlife Laboratories). Naltrexone has a longer half-life than the antagonist-agonist diprenorphine (Revivon, C-Vet Veterinary Products) and eliminates in- and posttransport renarcotization. Renarcotization is an effect that occurs when using opioids. Several hours after antagonist application, the animals once again come under the influence of the opioid agonist (Kreeger et al., 2002). Especially in equids captured in the wild this effect could be fatal as it potentially makes an individual more prone to predation and injury. However, it is important to note that because of the long half-life a subsequent anesthesia induction with ethorphine (or any other opioid), in case of emergency, would not be possible and an alternative method (e.g., the α_2 -agonist medetomidine and ketamine) needs to be considered (Table 46.4).

Chemical Capture of Equids in the Wild

Przewalski's Horses Because of the general lack of cover in the Gobi area, wild Przewalski's horses are extremely difficult to approach in the field. During the

 Table 46.4.
 Selected anesthetic protocols for wild equids.

Species	Drug 1	Drug 2	Additional drugs	Antagonist	Comments	Literature
Kulan (<i>E. hemionus</i>) 4.2 mg ethorphine	4.2 mg ethorphine	17 mg ACP	30 mg xylazine	6 mg diprenorphine +	total dose for adult	1
	0.016 mg/kg ethorphine	0.067 mg/kg ACP		0.042 mg/kg diprenorphine + 0.042 mg/kg diprenorphine + 0.4 mg/kg nalombine	n = 27 + 49	3,4
	5.4 mg ethorphine		150 mg ketamine	250 mg naltrexone	total dose for adult $n = 3$ -wild	
	4.4 mg ethorphine	10 mg butorphanol	10 mg detomidine	6 mg diprenorphine	n = 17 wild	6
Kiang (E. o. kiang)	0.012 mg/kg ethorphine	0.05 mg/kg ACP		0.025 mg/kg diprenorphine	n = 26 + 10	3,4
Somali wild ass (E. onager)	0.017 mg/kg ethorphine	0.07 mg/kg ACP		0.045 mg/kg diprenorphine	n = 14	3,4
Przewalski's horse (E. c. przewalskii)	0.008 mg/kg ethorphine	0.033 mg/kg ACP	0.033 mg/kg detomidine 0.033 mg/kg buthorphanol	0.16 mg/kg naltrexone + 0.04 mg/kg atipamezole IV	n = 34-wild	9
	0.018 mg/kg ethorphine	$0.075 \mathrm{mg/kg} \mathrm{ACP}$	0.16 mg/kg xylazine	0.045 mg/kg diprenorphine IV	n = 32 + 41	3,4
	0.07-0.1 mg/kg medetomidine	1.8-2.6 mg/kg ketamine		0.17-0.23 mg/kg Atipamezole	n = 11 from 14	2
	0.6 mg/kg romifidine	3.3 mg/kg TZ		tolazoline 2.5-3 mg/kg IV	n = 15	7
Mountain zebra	0.35 mg/kg romifidine	$1.8 \mathrm{mg/kg} \mathrm{TZ}$		tolazoline 2.5-3 mg/kg IV	6 = u	7
(E. zebra)	4–6 mg ethorphine	80 mg azaperone		9.6-14.4 mg diprenorphine	total dose for adult	1
	0.009–0.01 mg/kg ethorphine	0.037-0.044 mg/kg ACP		0.045 mg/kg diprenorphine IV	high dose for male $n = 53 + 69$	3,4
Plains zebra	0.0085-0.01 mg/kg ethorphine	0.035-0.04 mg/kg ACP		0.045 mg/kg diprenorphine IV	n = 54 + 21	3,4
(E. burchelli)	5.5-8.3 mg/kg TZ	0.06–0.08 mg/kg detomidine			n = 11 long recovery	5
Grevy's Zebra (Fauus grevvi)	0.01–0.017 mg/kg ethorphine	0.03-0.04 mg/kg detomidine	0.02-0.03 mg/kg ACP	100 mg naltrexone per mg of etorphine used IV		
(-/8						

ACP, acepromazine. TZ, Tiletamine/Zolazepam.

Naltrexone can be used at 20 to 50 mg per mg of etorphine and may be preferable to diprenorphine.

From (1) Kreeger TJ, ed. Handbook of Wildlife Chemical Immobilization. Laramie, WY: International Wildlife Veterinary Services, 1996; (2) Matthews NS, Petrini KR, Wolff PL. Anesthesia premiers resultats. Proc Int Symp Dis Zoo Wild Anim 1993:277-280; (6) Walzer C, Baumgartner R, Robert N, et al. 2000. Medical considerations in the reintroduction of the Przewalski Horse Zoobedingungen. Equus 1999;3:306–314; (5) Vitaud C. Utilisation de la combinaison anesthesique tiletamine/zolazepam et detomidine chez les zebres de Grant (Equus burchelli boehmi) of Przewalksi's horses (Equus przewalskii przewalskii) with medetomidine/ketamine and antagonism with atipamezole. J Zoo Wildl Med 1995;2:231–236; (3) Strauss G. Erfahrungen bei der Equus przewalskii) to the Dzungurian Gobi, Mongolia. Proc Eur Assoc Zoo Wild! Vet 2000: 147-150; (7) Walzer C. Unpublished data, 2002; (8) Wiesner H, von Hegel G. Zur Immobilisation immobilisation verschiedener Equidenarten in Tierpark Berlin-Friedrichfelde. Proc Int Symp Dis Zoo Wild Anim 1992;163–169; (4) Strauss G. Zur Immobilisation der Wildequiden unter von Wildequiden mit STH 2130 und Tiletamin/Zolazepam. Tierärztl Prax 1990;18:151–154; (9) Walzer C, Kaczensky P, Ganbataar O, et al. Capture and anaesthesia of wild Mongolian equids: the Przewalski's horse (*E. ferrus przewalsk*ii) and the Khulan (*E. Hemionus*). Mongol J Biol Sci, in press. past years we have employed various methods to get within shooting range such as approaching on a motorcycle and horseback or waiting at water points. Using a combination of 2.5 to 3.0 mg ethorphine, 10 mg detomidine, and 10 mg butorphanol, 14 horses have been successfully captured in the wild (and 35 procedures in the very large adaptation enclosures, 20-30 ha) in Mongolia (Walzer et al., 2006). Initial effects were noticed after 3 to 5 minutes when the animal exhibited a stiff, high-stepping gait and became ataxic. Induction to lateral recumbency occurred within 5–10 minutes. Procedures lasted on average 35 minutes. Following IV antagonist application anesthesia was smoothly reversed without any signs of excitement and the animals were back on their feet within 2 minutes. It is important to note that the head of all equids should be fixed to the ground as long as possible following antagonist application to prevent premature uncoordinated attempts at getting up, as these could result in injury (Walzer et al., 2006) (Figure 46.5).

Asiatic Wild Ass In Mongolia the wild ass is extremely skittish, probably because of poaching activities, and in some areas flees human presence at several kilometers distance (e.g., in Great Gobi B SPA). We have employed three distinct techniques to capture this species in the wild. In the summers of 2002 and 2005 we used a modified high-pressure CO₂ dart gun (Daninject JM) from a pre-placed hide, 60 to 80 meters distant from water points. This method was especially useful in the south Gobi as the khulan is readily approached in the area. Some water points additionally offer good cover that allows for a shooting distance of 40 to 55 meters. If possible, it is a distinct advantage to take a position high above the animal (e.g., cliff face), as they are unwary of danger from above. As open water is lacking in large

parts of the distribution range in the south Gobi, wild asses must dig to a depth of approximately 45 cm to access ground water. At this time it is very difficult for the animals to see movements in their vicinity. Furthermore, the use of ground water increases the amount of time the animals have to remain stationary, which additionally greatly facilitates darting.

In 2003 and 2005 we also employed a chase method in which the khulan was darted from a moving jeep. This method had previously been used to collar a wild Bactrian camel (Camelus bactrianus ferus) and is traditionally employed by wild ass poachers with 12-gauge shotguns (Blumer et al., 2002). When using the local UAZ jeeps it is important to remove the window from the passenger side and to provide seatbelts for the driver and shooter. If using the Daninject JM CO₂ dart gun, a short 4-cm barrel can be used instead of the standard barrel, as this greatly facilitates movement in the jeep. Once an animal is identified, it is chased till the jeep is able to approach within approximately 10 to 15 meters on a parallel track (Figure 46.6). It is then easily darted in the rump musculature using standard pressure settings. It is essential to define a chase cut-off time before the procedure is started. Our experience has shown that a cut-off time of 15 minutes is adequate for the Asiatic wild ass. To date we have captured 12 animals with this very time-efficient method. The shortest chase time was 2 minutes and the longest 13 minutes. In all cases induction was extremely rapid and smooth (4-8 minutes) and body temperature was below 40°C. A severe limitation to this method is that one is only able to capture males or juveniles without foals. A chase of a female with a foal would result in (permanent) separation of the young from the mare; therefore, it is unacceptable.

Finally we have used a video-enabled remote controlled CO_2 gun (Walzer & Boegel, 2003) at several water



Figure 46.5. The head of all equids should be fixed to the ground as long as possible following antagonist application to prevent premature uncoordinated attempts at getting up, as these could result in injury.



Figure 46.6. An Asiatic wildass being darted in the rump musculature from a moving jeep (60 km/h) at a distance of approximately 10 to 15 meters on a parallel track.

points in attempts to capture khulan in 2003 and 2005. To date this method has not been successful for wild ass mainly because of the abundance of water in the areas it was employed. In the author's view this method has great potential in areas with small water holes that the animals have to visit.

In all wild ass procedures, anesthesia was induced with a single 3-ml dart containing a combination of 4.4 mg ethorphine (M99), 10 mg detomidine–HCl (Domosedan) and 10 mg butorphanol (Torbugesic). Anesthesia was initially reversed with an IV combination of 200-mg Naltrexone and the α_2 -antagonist 20-mg Atipamezole. Reversal was rapid and generally smooth but some signs of excitation related to radio collar placement (head shaking) were noted. Subsequently, the opioid antagonist-agonist diprenorphine was used. This eliminated head shaking and provided a smoother reversal. All animals were standing and alert approximately 2 minutes following administration of the antagonists.

Zebras The chemical capture of zebras has been described previously (Burroughs, 1993a). Similar to the Asiatic wild equids, zebras are very difficult to approach in the wild. The techniques employed are similar to the ones described in the preceding. When available, darting from a helicopter is recommended (Burroughs, 1993a).

Chemical Capture of Captive Non-domestic Equids

Carfentanil has been extensively studied as an immobilizing agent for non-domestic equids (Allen, 1992, 1994, 1997; Klein and Citino, 1995). Ethorphine was not available to zoo and wildlife veterinarians working in the United States for several years, so carfentanil was used as a primary immobilizing agent for non-domestic equids (Allen, 1992, 1994, 1997). There are several disadvantages of using carfentanil versus ethorphine as an immobilizing agent for non-domestic equids. Often times non-domestic equids immobilized with carfentanil have to be assisted into recumbency or be given supplemental anesthetic induction agents to achieve complete immobilization (Allen, 1992, 1994; Klein and Citino, 1995). Supplemental anesthetic agents are given IV after the animal is partially immobilized by carfentanil. Ketamine, glyceryl guaiacolate (guaiphenesin), or propofol is often used to get adequate muscle relaxation and complete immobilization (Allen, 1992, 1994, and 1997). The delivery of carfentanil by dart into the muscles of the neck or shoulder results in faster induction times and less anesthesia-related morbidity (Allen, 1992, 1994, 1997). Significant respiratory depression is commonly seen with carfentanil immobilizations (Allen, 1992 and 1994). This can be successfully treated with IV administration of doxapram and the delivery of intranasal oxygen (Allen, 1992, 1994, and 1997). Most

non-domestic equids immobilized with carfentanil alone experience significant tachycardia, which may be caused by the stress of the procedure and inadequate immobilization (Allen, 1992, 1994). Additionally, renarcotization may occur in non-domestic equids immobilized with carfentanil.

Re-narcotization seems to be more common in the Somali wild ass (*Equus onager*) when immobilized with carfentanil (Allen, 1997). Carfentanil, when used alone, was not adequate for the immobilization of Grevy's zebra (*Equus grevyi*) unless unacceptably high doses were used (Allen, 1997).

Grevy' zebra (*Equus grevyi*) can be immobilized with carfentanil in combination with other drugs in a staged immobilization protocol (Klein and Citino, 1995). First, detomidine (0.1–0.15 mg/kg) is given IM. Then approximately 20 minutes later carfentanil (0.0098 mg/kg) in combination with ketamine (2 mg/kg) is given IM. In one study, this combination was compared with medetomidine and ketamine in combination. Both study groups experienced significant hypertension with these combinations (Klein and Citino, 1995). The preferred method for immobilizing captive Grevy's zebra is using ethorphine in combination with detomidine or detomidine and acepromazine (Table 46.4).

Although carfentanil can be used to immobilize captive non-domestic equids, ethorphine is the preferred primary immobilizing agent. Diprenorphine, in most cases, will adequately antagonize the effects of ethorphine. However, in one comprehensive review of renarcotization in non-domestic equids, renarcotization was relatively common in zebra and onager when using diprenorphine to antagonize ethorphine (Allen, 1990). The use of naltrexone to antagonize ethorphine typically does not result in any episodes of renarcotization in non-domestic equids.

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47 Tapirs

Sonia M. Hernandez-Divers and James Bailey

INTRODUCTION: TAXONOMY AND NATURAL HISTORY

Tapirs belong to the family tapiridae, within the order Perissodactyla, which are distinguished from the Artiodactyla by their foot morphology and digestive system. Their closest relatives are rhinoceroses and horses. The small family of tapiridae has only four species within the single genus Tapirus. There are three New World species (T. terrestris, T. bardi, and T. pinchaque) and a single Old World species (T. indicus). Tapirs are typically solitary (except mother and offspring pairs), largely nocturnal, tropical forest herbivores. In the wild, tapirs spend most days sleeping in dense areas and forage at night. They often inhabit aquatic habitats, spending large amounts of time in or near water (Klingel and Thenius, 1990; Nowak, 1991). Further, they are found to frequently urinate and defecate in water. These are all proposed as passive, stealth defense mechanism for survival. Despite their size, they can travel very quietly in the forest, are extremely agile, can run fast, and if threatened or protecting offspring, will charge (Hernandez-Diver, personal observation).

All species except the mountain tapir (*T. pinchaque*) are commonly exhibited in zoological institutions. To date, both captive and free-ranging individuals of all four species have been physically and chemically immobilized; however, the protocol used, and its success, varies with capture situation. Therefore, no one anesthetic protocol is recommended for all situations.

CLINICAL ANATOMY AND PHYSIOLOGY

A variety of sources have reviewed the anatomic peculiarities of tapirs (Janssen, 2003); therefore, details provided here are limited to those relevant to physical or chemical restraint. Table 47.1 summarizes the body weight and sizes for each species of Tapiridae. As with any animal of that size and weight, rough induction or

recoveries can lead to severe, often untreatable, traumatic injuries and safety concern for personnel. Unlike horses, tapirs do not kick, but can inflict severe injury by biting, stomping and charging. The dental formula for tapirs is 2x (I-3/3, C-1/1, P-4/3, M-3/3). The upper third incisor is large, and separated from the canine by a narrow diastema, which allows the manipulation of the tongue in the anesthetized animal. The glottis of the tapir is similar to the horse. Therefore, blind or laryngoscope-assisted intubation is possible (Figure 47.1). Pulmonary atelectasis, ventilation-perfusion mismatch, or neuropathies associated with prolonged recumbency can complicate anesthetic procedures. The anesthetists are encouraged to review principles of large animal anesthesia when planning an immobilization procedure to minimize these risks as much as possible (Steffy, 1990; Muir and Hubbell, 1991). Supplemental oxygen, assisted ventilation, and appropriate padding should be considered even in field captures. Tapirs, like horses, are unable to vomit; however, regurgitation is still possible. Tapirs are hindgut fermenters, with small stomachs and large cecum and colons. Much like horses, tapirs can be at risk for gastrointestinal disease following chemical immobilization. Tapirs have a highly mobile proboscis that acts as a tactile and prehensile organ. The proboscis is a fleshy organ lacking any internal osseocartilaginous support, constructed of connective tissue and muscle (Witmer, Sampson, and Solounias, 1999). This organ is highly sensitive and care should be taken not to restrict its movement during immobilization or cause it injury during anesthesia.

PHYSICAL CAPTURE AND IMMOBILIZATION

Despite their large size, tapirs have had a reputation of being docile in captive environments and extremely elusive as free-ranging animals. In free-ranging situations tapirs are adept at hiding, are extremely quiet when moving even in dense habitats and generally stay

Table 47.1. Typical body weight and size for members of Tapiridae.

Species	Body Weight (kg)	Body Length (cm)	Height at Shoulder (cm)
Tapirus bairdii (Baird's tapir)	150-300	198-202	Up to 120
Tapirus terrestris (Lowland tapir)	250-300	180-250	77-108
Tapirus pinchaque (Mountain tapir)	225-250	180	75-80
Tapirus indicus (Malayan tapir)	200-375	185-240	90-105

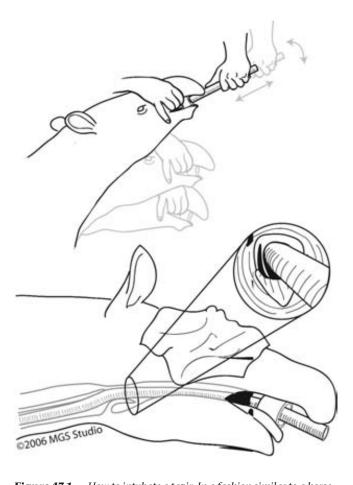


Figure 47.1. How to intubate a tapir. In a fashion similar to a horse, intubation is preformed in the tapir, with ease, blindly. Optimally the tapir's mouth is flushed with water to remove debris prior to anesthesia. In the field the only opportunity to remove debris may be after anesthetic induction by a brief finger sweep of the buccal surfaces and examination of the oropharynx. After induction of anesthesia the tapir is moved to lateral recumbency. The optional mouth speculum (PVC pipe segment) may be placed between the upper and lower incisors and the head extended to create a linear oral-laryngeal-pharyngeal axis. The endotracheal tube is then passed through the mouth speculum, over the base of the tongue into the pharynx. The tube may pass immediately into the larynx and trachea. More frequently it is necessary to hold the head in extension, retract the endotracheal tube 10-15 cm, rotate the tube on its axis 45-90 degrees and advance to the larynx once more. Multiple gentle rapid advancements and retractions, lightly tapping on the laryngeal opening will usually lead to intubation. Changing the degree of extension of the head while advancing the endotracheal tube may be of assistance. In the event blind intubation fails, a long-bladed laryngoscope may be used for direct laryngoscopic examination to intubation. Endotracheal tubes from 16 to 20 mm inside diameter (cuffed) are appropriate for adult tapirs. (Reproduced with permission. Bailey J, Hernandez-Divers S. Immobilization and evaluation of oscillometric blood pressure monitoring during of free-ranging Baird's tapirs (Tapirus bairdii) in Costa Rica. JAVMA in press.)

out of sight. Reports of tapir captures for ecological studies include attracting the animal to bait stations, pitfall traps, box traps, capture pens and using dogs for locating and chasing an individual animal (Foerster et al., 2000; Hernandez-Divers and Foerster, 2001; Mangini, Velastin, and Medici, 2001; Mangini and Velastin, 2001; Medici et al., 2001). All capture techniques reported were followed by chemical immobilization.

As opposed to similarly sized mammals maintained in captivity, tapirs have traditionally been managed through direct contact. A recent report of severe biting and crushing injuries inflicted on a zoo keeper should caution tapir handlers of the safety implications when attempting physical immobilization. When provoked, even free-ranging tapirs can inflict fatal injuries and at least one report exists of a tapir that killed a farmer that stabbed the animal because it was eating his crops (Haddad, Assuncao, and de Mello, 2005). Therefore, current Association of Zoo and Aquarium standards recommend that tapirs are managed following guidelines for protected contact, where caretakers do not go inside enclosures with the animals (Shoemaker et al., 2004). The only acceptable type of physical immobilization, which requires additional training, is the use of a large animal chute (Janssen, 2003).

Tapirs are amenable to training using positive reinforcement techniques. Additionally, they can be scratched-down, a technique that involves using a horse brush or outdoor broom to stroke the animal's dorsum, neck, and lateral and abdominal walls (Janssen, 2003). This appears to induce a pleasurable state in which the animal first sits, and then lays down in lateral recumbency. Although tapirs apparently enjoy this interaction, the level of immobilization induced should not be over-emphasized. This technique, alone or combined with de-sensitization training, has been used for physical examination and blood collection, and can be used to administer injections. Positive reinforcement has also been used to move animals from one area to another, to enter crates, present body parts for examination, and stand still for biological sample collection and intravenous (IV) catheterization.

CHEMICAL IMMOBILIZATION

Historically, tapirs were anesthetized using potent opioids; however, the recent increase in use of α_2 -adrenergic agonists alone or in combination with other drugs has

Table 47.2. Criteria that should be considered when designing an anesthetic protocol for tapirs.

Criteria	Free-Ranging	Captive
Anesthetic onset Reversible anesthetic	Rapid induction (avoid predation, trauma, drowning) Fully reversible	Not as crucial, as animal is typically confined Not as crucial, as animal is typically confined
Anesthetic safety	Wide margin of safety (pre-capture body wt may not be available)	Wide margin of safety (disease is a more common indication for anesthesia in captivity)
Cost	Relatively inexpensive	Expense concerns vary
Volume	Volume should be minimized for remote delivery	Volume not as crucial, as dart distance is typically short

decreased the need for drugs like etorphine and carfentanil. In fact, the use of those drugs has been largely abandoned in tapirs, as they produced poor oxygen saturation (Janssen, 2003) and a safety risk to personnel. The anesthetic protocol preferred may depend on whether the animal is captive or free ranging. Table 47.2 summarizes the major concerns in both cases.

PRE-ANESTHETIC CONSIDERATIONS

As with any animal, tapirs that are calm are better candidates for anesthesia. The physiological effects of excitement and endogenous release of catecholamines may delay or prevent anesthetic induction or muscle relaxation. In fact, the success of some anesthetic protocols used for free-ranging tapirs depend on the animal's degree of relaxation (Foerster et al., 2000; Hernandez-Divers and Foerster, 2001). In all cases, it is important to create a quiet environment while working with these animals. If the animals cannot remain stress free (i.e., transport, trauma, or disease), pre-anesthetic medication is highly recommended. Tapirs are often maintained in enclosures with bodies of water and when threatened, they often retreat into the water. This must be taken into consideration when planning an anesthetic procedure. In free-ranging situations, capture protocols are designed to specifically avoid drowning by either anesthetizing animals that are contained, or are at least 200 m away from a body of water (Foerster et al., 2000; Hernandez-Divers and Foerster, 2001). To maximize safety, capture techniques should be designed to minimize the probability an animal will walk or run after anesthesia has been administered. Although vomiting is generally not a consideration, fasting for 24 hours prior to anesthetic procedures is recommended. This decreases the amount of food within the oral cavity and esophagus; minimizes the probability of regurgitation, and minimizes the pressure on the diaphragm related to the gastrointestinal tract distention secondary to fermentation of food material during the anesthetic period (Andersen et al., 2006). Tapirs are tropical animals; therefore, in regions with cold climate, they should be maintained in an indoor area that can be heated prior to the anesthetic period. In warmer climates, hyperthermia is a concern; therefore, procedures should be planned for early morning, and methods to prevent and

decrease excessive body temperatures should be available. Regardless of temperature concerns, tapirs should not be anesthetized in full sun, as their skin is sensitive to sunburn. If previous training allows, the length of the anesthetic period may be minimized by collecting samples or placing IV catheters ahead of time; however, this must be carefully balanced with the stress these procedures can cause. Whenever possible, it is important to obtain a resting heart, respiratory rate and body temperature on each individual to use as baseline for comparison during anesthetic monitoring.

PRE-ANESTHETIC MEDICATION AND INDUCTION

Although the administration of pre-anesthetic medication is not routine in tapirs, in horses it is standard, if not mandatory, practice (Muir and Hubbell, 1991; Martinez et al., 2006). Pre-anesthetic agents provide tranquilization, reduce the amount of induction and maintenance anesthetic agents required, balance the anesthetic technique to limit negative side effects, and may contribute to smooth recoveries. The common equine preanesthetic agents xylazine and butorphanol have been applied successfully in tapirs (Foerster et al., 2000; Hernandez-Divers and Foerster, 2001). An estimated dosage of 0.15 to 0.25 mg/kg butorphanol combined with 0.3 to 0.5 mg/kg xylazine delivered IM produced immobilization of tapirs. This dosage would provide sedation but not recumbency of a horse. Routine mild to moderate sedation of a horse would require xylazine 0.3 to 0.5 mg/kg and butorphanol 0.01 to 0.02 mg/kg IV. Intramuscular dosages of up to 2 mg/kg xylazine, with and without butorphanol have been used for moderate to profound sedation of horses (Muir and Hubbell, 1991). The apparent greater sensitivity of the tapir to these common equine pre-anesthetic agents suggest a lower dosage could be used if only mind sedation were desired.

Induction is typically achieved through remote means (free-ranging and captive) or IV routes (captive) (Figure 47.2). When anesthesia is induced in tapirs they behave similarly to the horse, with some minor differences. Initially they stand still, often in a saw-horse position, with limbs further apart than normal and drop their head. Tapirs may drool and lose control of their proboscis. From this position, they often sit, in a



Figure 47.2. One method of immobilizing free-ranging tapirs. Bananas are placed in the center of a bait station. Additional bananas are thrown from a chosen location, such as this tree platform, into the forest and hung from nearby trees to disperse the odor of bananas for several days. Once evidence of tapir visitation is noted (tracks), captors sit at the proven bait station, starting at dusk (Foerster et al., 2000.). Tapir movements are often not detected until the animal is with 20 meters of the captors. Once an animal's footsteps are heard, a low-power flashlight or a night-vision telescope is used to scan the area and confirm that the animal is a tapir. Immobilization drugs are then prepared while additional bananas are dropped every 10 to 20 seconds to bring the animal closer to the captors. This feeding technique distracts the tapir while the dart is being loaded and entices the tapir to move to an area for an advantageous dart shot. The tapir's reaction to thrown bananas is also used to evaluate its demeanor and level of nervousness. When the dart is loaded and the tapir is in an acceptable location for darting, a final decision is made regarding behavior and likely reaction to dart impact. A low-power flashlight may be used to transiently illuminate the tapir (if night vision is unavailable) and the tapir is darted. (Reproduced with permission. Bailey J, Hernandez-Divers S. Immobilization and evaluation of oscillometric blood pressure monitoring during of free-ranging Baird's tapirs (Tapirus bairdii) in Costa Rica. JAVMA in press.)

dog-like position, and then move to sternal recumbency (Figure 47.3). In some cases, they remain standing and may need some light pressure on the hindquarters to encourage sitting. Table 47.3 reviews reported protocols for immobilization of free-ranging tapirs.

A wide range of drug combinations have been reported for use in captive tapirs. Table 47.4 summarizes the protocols used in captivity.

Despite their thick skin, a variety of peripheral vessels can be used in tapirs for administration of IV agents. Based on the author's experience and previous reports, the marginal auricular vein, carpal and medial saphenous veins can be used for both blood collection or short-term catheterization (Janssen, 2003). IV induction is rarely used, but can be accomplished in trained individuals. Standing sedation, using xylazine or other α_2 -agonist combinations, should be considered for short procedures that require little manipulation (i.e., skin biopsy, blood collection, portable radiography,

etc.). Standing sedation using azaperone (1 mg/kg IM) has also been reported (Janssen, 1996).

MAINTENANCE ANESTHESIA

Typically, general anesthesia is maintained in horses by inhalation anesthetics or total intravenous anesthesia (TIVA). Isoflurane, and sevoflurane and halothane are all commonly used inhalation anesthetic agents for horses (Muir and Hubbell, 1991; Martinez et al., 2006). To date, isoflurane is the most common inhalant used in for maintenance of anesthesia of tapirs, but the use of sevoflurane in the future is anticipated. Mixtures of injectable anesthetic agents, such as the classic xylazine, ketamine, and guaifenesin (also known as triple-drip) may be used to maintain general anesthesia for relatively short procedures in horses, but no reports exist in tapirs (Aubin and Mama, 2002). Propofol, although not routinely used in large animals, is an acceptable TIVA

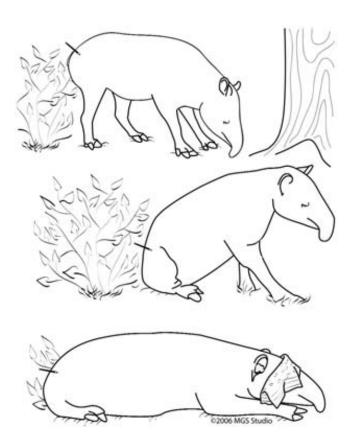


Figure 47.3. Typical induction behavior of a tapir. The tapir getting drowsy; head-down with a base-wide (saw-horse) stance: (1) leaning back slightly and proboscis extended; (2) down to a sitting position with forelimbs extended; and (3) down in sternal recumbency (on its stomach), now with a blindfold applied over its eyes and gauze sponges placed in its ears (to reduce ambient sound stimulus). (Reproduced with permission. Bailey J, Hernandez-Divers S. Immobilization and evaluation of oscillometric blood pressure monitoring during of freeranging Baird's tapirs (Tapirus bairdii) in Costa Rica. JA VMA in press.)

method for horses. Constant rate infusions of propofol have been reported in tapirs (Hernandez-Divers and Foerster, 2001). Horses anesthetized with either isoflurane or propofol experience cardiopulmonary depression in a dose dependent fashion. Propofol is more likely to lead to apnea than isoflurane (Mama, Steffey, and Pascoe, 1995, 1996; Reid, 1997).

MONITORING AND ANESTHETIC SUPPORT

Once anesthetized, tapirs can be maintained in sternal or lateral recumbency. However, sternal recumbency allows for better ventilation in large animals (Steffy et al., 1990; Steffy, Woliner, and Dunlop, 1990). A blindfold should be applied to protect the corneas, as corneal edema, suspected to be associated with prolonged exposure to ultraviolet radiation, has been reported in tapirs (Janssen, 2003). Gauze should be inserted into the ears to decrease auditory stimulus. Premature arousal can occur with excessive noise, particularly when using

 α_2 -agonist combinations. Minimally, heart rate, peripheral pulse strength, respiratory rate, and body temperature should be monitored as with any other large animal.

Pulse oximetry is best accomplished by applying the probe to the tongue, ear, or rectum. Although the oxygen-hemoglobin disassociation curve has not been determined for tapirs, the curve for horses (p50 = 25mmHg) indicates that a 90% saturation reading on the pulse oximeter is approximately equal to an arterial partial pressure of oxygen of 60 mmHg, which is distinctly hypoxemic (Clerbaux et al., 1993). Therefore, saturation levels as measured by a pulse oximeter should be maintained well above 90% (i.e., 95%-100%). Even in healthy animals, heavy sedation and general anesthesia frequently lead to a fall in the arterial partial pressure of oxygen (PaO₂). This is particularly true of larger animals, and only in part owing to hypoventilation. Importantly, ventilation to perfusion mismatching increases dramatically in anesthetized large animals (Muir and Hubbell, 1991). To compensate for hypoxemia, the use of nasal oxygen (10-15 L/minute) should be considered. As blind intubation of the tapir is accomplished with relative ease (adult tapir: 16-20 mm internal diameter endotracheal tube), intubation with tracheal insufflation of oxygen, or positive pressure ventilation (20-30 cm H₂O) are reasonable solutions. Improved oxygen saturation and ventilation may be accomplished in the field using a demand valve driven by 100% oxygen, or a manual resuscitator bag with supplemental oxygen attachment (Ambu A/S). Only one report of the aforementioned protocols assessed the cardiopulmonary effects in detail (Foerster et al., 2000). In that report, hypoxemia was noted and supplemental oxygen was recommended. Blood gases can be monitored by sampling the facial, auricular, or medial saphenous arteries (Figure 47.4).

Blood pressure can be measured indirectly through the use of blood pressure cuffs on the limbs. Direct blood pressure measurements can be achieved most readily with the use of a 22-gauge catheter placed in the readily accessible auricular artery. A study that compared the usefulness and accuracy of indirect versus direct blood pressure monitoring methods in tapirs found that indirect blood pressure measurements using an oscillometer blood pressure monitor correlated with direct readings, indicating that this is a valid method to measure blood pressure in tapirs (Bailey, Foerster, and Foerster, 2000) as measured within the limits of pressure ranges examined (field conditions).

Base-apex lead electrocardiograph application simply requires a positive lead caudal to the heart apex and a negative lead cranial to the heart base. Those unaccustomed to the base-apex lead are often perplexed by its classic description. A less confusing base-apex lead places the left leg lead caudal to the heart apex (left sternal border), the right arm and left arm leads cranial to

Table 47.3. Summary of protocols utilized to immobilize free-ranging tapirs.

Geographic Location	Species	Capture Method	Anesthetics	Comments
Costa Rica	Tapirus bairdii	Attracted animals to bait stations	Etorphine 1.88 mg and 7.7 mg acepromazine IM per animal; Reversal: Diprenorphine hydrochloride at 3 X the etorphine used	Administered to animals from a tree blind via a dart. The animals had been habituated to come to bait (ripe bananas) for several days and thus were relatively calm when darted (Paras, 1996)
Costa Rica	Tapirus bairdii	Attracted animals to bait stations	Total dosage for a 200–300 kg animal: 40–50 mg of butorphanol and 100 mg of xylazine in the same dart. Additional ketamine (187 ± 40.86 mg/animal) or constant rate infusion of propofol (50–200 mcg/kg/min), administered IV. Reversal: Naltrexone–50 mg IM with 1200 mg of tolazoline in the same syringe IM; no sooner than 30 min from last administration of ketamine.	Administered to animals from a tree blind via a dart. The animals had been habituated to come to bait (ripe bananas) for several days and thus were relatively calm when darted. Animals weight estimated between 200–300 kg. Average time to sternal recumbency: 11 min. Average return to standing after reversal: 12 min. (Foerster, 2000)
Venezuela	Tapirus terrestris	Immobilized animals were captive, semi-captive or wild tapirs	Ketamine (3.5–4 mg/kg) and Xylazine (2–2.2 mg/kg) IM supplemented with Ketamine (1.4 mg/kg) IM; Reversal: Tolazoline 4 mg/Kg	Administered using darts projected by a blowpipe, or IV using syringe (Blanco, 2004).
Venezuela	Tapirus terrestris	Immobilized animals were captive, semi-captive or wild tapirs	Telazol (2.5–2.8 mg/kg) supplemented with Ketamine (1.2–1.5 mg/kg) IM; Reversal: Tolazoline 4 mg/Kg	Administered using darts projected by a blowpipe, or IV using syringe (Blanco, 2004).
Mexico	Tapirus bairdii		Total dosage for a 200–250 kg animal: 1.96 mg Etorphine hydrochloride and 5.90 mg of Acepromazine maleate, in the same dart; Reversal: Diprenorphine hydrochloride 5.88 mg	This protocol was designed for specific environmental conditions (slopes of more than 60 degrees) of the Sierra Madre. Induction times minimized to avoid fatalities (pers comm, Ivan Lira Torres, 2006, modified from Paras, 1996; Kreeger, 1997)
Brazil	Tapirus terrestris	Captured in pens or pit–falls	Butorphanol tartrate (0.15 mg/kg) with Medetomidine (0.03 mg/kg) IM, in same dart; Reversal: Atipamezole (0.06 mg/kg) with Naltrexone (0.6 mg/kg) in same syringe, IV	Adequate chemical restraint for radio collaring, and biological sampling. Average induction time: 10 min (Velastin, 2004)
Brazil	Tapirus terrestris and Tapirus pinchaque	Captured in pens or pitfalls, or immobilized by dart	Dosages were calculated using allometric scaling: ketamine (0.62–0.41 mg/kg) and atropine (0.025–0.04 mg/kg), and tiletamine zolazepam (1.25–083 mg/kg), and romifidine (0.05–0.03 mg/kg) OR detomidine (0.06–0.04 mg/kg) OR medetomidine (0.006–0.004 mg/kg) in the same dart; Reversal: atipamezole 0.06 mg/kg.	Average induction time: 5 min. Medetomidine produced best results obtaining good muscular relaxation and more stable cardiopulmonary parameters (Mangini, 2001a,b)

the heart base on the neck in the right jugular furrow, with the ECG monitor set for lead II (often the default setting). This produces a base-apex lead electrocardiogram similar in appearance to the standard lead II. Species with a diffuse Purkinje fiber network produce a unique mean electrical axis. A simple rule of thumb states that if the animal is small or its ancestors were small it is likely to have a type I heart with a less diffuse Purkinje network, caudally oriented mean electrical axis, and primarily positive wave form in lead II, such

as seen in dogs and cats. If the animal is large or its ancestors were large it is likely to have a type II heart with a diffuse Purkinje network, cranially oriented mean electrical axis, and primarily negative wave form in lead II, such as seen in the horse and the tapir (Figure 47.4) (Muir and Hubbell, 1991).

Temperature is typically monitored through a rectal thermometer. The depth of anesthesia can be monitored subjectively much as in a horses. Ideally, at a moderate plane of anesthesia, muscles should be relaxed

Table 47.4. Anesthetic protocols used in captive tapirs.

Type of Facility	Species	Anesthetic Protocol Used	Comments
Zoological institution	Tapirus pichanque	Carfentanil (5.4 µg/kg), ketamine (0.26 mg/kg) and xylazine (0.13 mg/kg) IM; Reversal: yohimbine (0.2 mg/kg IV) and naltrexone (100–200 mg/kg, half IV, half SC)	Six immobilizations of tapirs (1 female, 3 males; 1 juvenile male immobilized 3 times) for footwork, gastrointestinal endoscopy, reproductive surgery (Miller–Edge, 1994)
Zoological institution	Tapirus indicus	Butorphanol (0.15 mg/kg) and detomidine (0.05 mg/kg) OR xylazine (0.3 mg/kg) all IM; use ketamine if needed (0.5 mg/kg IV); Reversal: naloxone and yohimbine (0.2–0.3 mg/kg IV)	Nineteen immobilizations of Malayan and mountain tapirs (Janssen, 1996)
Zoological institution	Tapirus bairdii	Acepromazine (7.7 mg/animal), butorphanol (0.13–0.2 mg/kg), detomidine (0.065–0.13 mg/kg) and ketamine (2.2 mg/kg) IM; No reversal	(Trim, 1998)
Zoological institution	Tapirus indicus	Etorphine 2.45 mg and acepromazine 10 mg total IM, then guaifenesin IV until intubation was possible; then isoflurane maintenance	18-month-old female; estimated to weigh 265 kg; immobilized for diagnosis and surgical management of abdominal abscess (Lambeth, 1998)
Zoological institution	Tapirus indicus	Butorphanol (80 mg IM) and Xylazine (120 mg total IM) OR detomidine (12 mg total IM); Reversal: naltrexone (200 mg total IM), tolazoline (1400 mg total IM)	Estimated body wt 340 k; repeated immobilizations of light anesthesia for diagnosis and treatment of oral squamous cell carcinoma (Miller, 2000)
Teaching hospital	Tapirus terrestris	Detomidine (0.03 mg/kg PO), 20 min later, carfentanil (1.85 μg/kg PO)	One animal repeatedly immobilized for wound management; variety of combinations of α_2 -agonist/etorphine or carfentanil were used but eight immobilizations with detomidine/ carfentanil PO were most useful (Pollock, 2003)

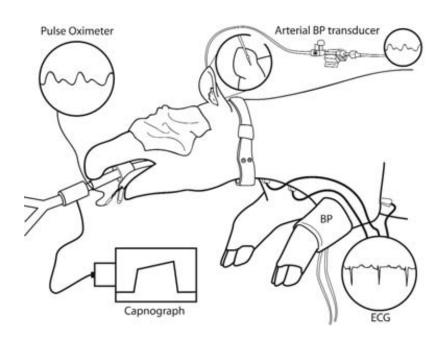


Figure 47.4. Vigilant monitoring of the tapir. Seen here: Lingual transmittance pulse oximeter and associated plethysmographic waveform; side stream (diverting) capnography and capnogram; non-invasive, oscillometric arterial blood pressure monitory (BP cuff); invasive (direct) arterial blood pressure monitoring through a blood pressure transducer with associated arterial waveform; base-apex lead electrocardiogram. (Reproduced with permission. Bailey J, Hernandez-Divers S. Immobilization and evaluation of oscillometric blood pressure monitoring during of free-ranging Baird's tapirs (Tapirus bairdii) in Costa Rica. JAVMA in press.)

even when stimulation is applied, the animal should breath in a regular manner with chest excursions that approximate a conscious animal, the position of the eye should be central and there may be a very slight palpebral reflex. The corneal reflex should remain until very deep planes of anesthesia.

RECOVERY

To avoid rough recoveries and minimize the cardiopulmonary effects of anesthetic agents, protocols that allow for their antagonism are preferred. Protocols that include α_2 -adrenergic agonists are typically antagonized well and lead to smooth, uneventful recoveries. If supplemental ketamine (or related drugs) is used, it is recommended that the reversal agent not be administered until at least 30 minutes have elapsed, to allow for redistribution of the drug. In free-ranging situations, maintaining containment of the tapir (in trap, or pitfall) can allow the animal to fully recover before release. In cases in which this was not possible, authors reported following the recovered animals for a period of time to monitor signs of ataxia, depression, or renarcotization (Foerster et al., 2000). In captivity, animals should be maintained in a quiet, dark, enclosed area until fully recovered. In all cases, the animal should be allowed to recover in the shade. Tapirs that are recovering from anesthesia typically begin by twitching their ears, moving the tongue in and out of the mouth, followed by return to sternal recumbency. From sternal recumbency they may first sit on the hindquarters or fully stand. Many tapirs begin walking in reverse as they gradually regain orientation to their environment. Horses recovering from inhalation anesthetics often experience dysphoria and are prone to self-inflicted trauma; therefore, additional sedatives or tranquilizers are often administered prior to recovery to buy time for inhalation anesthetic washout (Muir and Hubbell, 1991; Martinez et al., 2006). Tapirs undergoing prolonged surgical procedures (beyond metabolism of injectable induction agents) may need similar treatment. If sedatives are administered, horses, as with tapirs, tend to roll to sternal recumbency and sit in a controlled pause for several minutes prior to standing directly. Ideally the horse stands steady or walks with intent with limited ataxia. Ataxia has been reported in tapirs recovering from anesthetic protocols that included ketamine, emphasizing the need for containment and monitoring.

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48

Rhinoceroses

Robin W. Radcliffe and Peter vdB. Morkel

THE RHINOCEROTIDAE

Introduction

Like the fabricated creature in Albrecht Dürer's famous lithograph, the rhinoceros has long been a source of mystery, myth and intrigue (Figure 48.1). Part unicorn and part armored beast, the current knowledge of rhinoceros anesthesia likewise represents a melding of pure art and hard science. Today rhinoceros anesthesia is relatively commonplace, yet no less demanding in practice.

The Rhinocerotidae are truly living fossils—a remnant and archaic mammalian family represented by only five extant species in four genera restricted to Africa and Asia. The relic survivors belie a one-time place of dominance among organismic groups with over 150 fossil rhinoceros species discovered by paleontology across four continents (Prothero, 2005). Today, however, four of the five rhinoceroses are critically endangered from poaching and loss of habitat (Foose and van Strien, 1997; Emslie and Brooks, 1999).

Field anesthesia made possible the rhinoceros conservation success stories of the twentieth century (Harthoorn and Lock, 1960; Player, 1972; Meadows, 1996) and remains a critical tool for proactive rhinoceros management programs incorporating translocation, earnotching, radiotelemetry, microchip implantation, and other techniques designed to secure the conservation of both African and Asian species (Dinerstein, 1990, 2003; Kock, 1990, 1995). Historical and current rhinoceros anesthesia protocols are based on highly effective reversible opioid combinations, yet new anesthesia techniques continue to improve efficacy and safety for both animals and human personnel (Bush, 2005; Bush and Citino, personal communication).

Taxonomy and Evolutionary History

The odd-toed ungulates of the order Perissodactyla include three living families: the rhinos, horses, and tapirs. As the order name denotes, all Perissodactylids bear weight on one (equids) or three (rhinos and tapirs)

digits. Rhinos and tapirs are among the most primitive of the world's large mammals and are further grouped into the suborder Ceratomorpha based on a similar ancient body plan. The stout body of the rhinoceros is graviportal or designed for weight bearing with limb modifications to support large mass rather than the long angular limbs of equids in the suborder, Hippomorpha, specialized for speed.

The Perissodactyla enjoyed a period of extraordinary diversity in the Eocene epoch 34 to 55 million years ago before climate change presumably limited species radiation, culminating in extinction of 10 of the 14 perissodactyl families by the end of the Oligocene epoch (Radinsky, 1969). Prehistoric rhinoceroses in particular, as interpreted from fossil evidence, represented a far expanded group of organisms than exist today and included both horned and hornless forms. In fact, rhinoceroses were once the most common large herbivore in North America for most of the last 50 million years (Prothero and Schoch, 2002). An extinct hornless rhinoceros named Paraceratherium (also classified as Indricotherium) is known to science as the largest land mammal that ever lived, measuring over 6 meters at the shoulder and weighing an estimated 20 tons (Prothero and Schoch, 2002; Prothero, 2005).

Biology and Morphology

The Rhinocerotidae are large terrestrial herbivores that have evolved either a browsing (black, Sumatran, Javan) or grazing (white, greater one-horned) strategy to process large quantities of fibrous feeds or simple grasses, respectively. As such, they share bulky elongated skulls, dental patterns largely devoid of canines and incisors (retained to various degree in the Asian species), and prehensile or wide, flat lips in the browsers and grazers, respectively. Like the equids, fermentation takes place in the cecum and colon. The rhino gut is less efficient than that of ruminants since the microfloral protein formed in the hindgut is largely unavailable to the animal. As a result rhinoceroses must eat more, have



Figure 48.1. The famous 1515 drawing by German artist Albretch Dürer, a rhinoceros portrayal that persisted in Europe for three centuries despite the anatomical errors suggesting a mythical unicorn heritage. (Image copyright The Trustees of the British Museum, London.)

a relatively fast passage of gut contents, and possess limited time to reabsorb water from the feces. Therefore, rhinoceroses must drink every day or every second day, making it a water-dependent species rarely found more than 15 km from a water source.

Despite their often conspicuous absence in many fossil rhinoceroses, the single horn (*Rhinoceros* sp.) or pair of horns (*Ceratotherium*, *Diceros*, and *Dicerorhinus* sp.) is certainly the most distinguishing feature of the living Rhinocerotidae, giving name to the group literally as the *Nose-horned beasts* (Prothero and Schoch, 2002). Rhinoceros horns differ from true horns of the Artiodactyla by having no central core of bone. Instead the tubular hair-like keratin filaments are compressed in a linear fashion and set upon a bony protuberance of the skull. Underneath the horns, the skull incorporates extensive nasal bones and sinuses; structures inordinately prone to complications from trauma during capture and translocation.

Rhinoceros skin is thick (several centimeters of primarily collagenous dermis) (Cave and Allbrook, 1958; Shadwick, 1992), with the Asian species sporting subdermal plates and heavy skin folds, making skin anatomy an important consideration for remote drug delivery in the rhinoceros. The greater one-horned rhinoceros of Asia is perhaps best known for the exaggerated armor-like plates or folds first popularized in the famous Dürer woodcut of the Middle Ages (Figure 48.1). However, the epidermis is very thin (1 mm) and heavily keratinized, incorporating extensive vasculature, which may predispose the rhinoceros to pressure necrosis, particularly in calves (Cave and Allbrook, 1958; Gandolf, 2006). Significant body hair is an antiquated trait

retained in only one living species, the Sumatran or "hairy rhinoceros," so-called for its shaggy coat of hair (Figure 48.2). Wild *Dicerorhinus* have shorter more bristly coats than their captive relatives, a trait providing protection for the skin from the numerous biting insects that share its environment. Hair, a primordial trait of many fossil rhinoceroses, including the woolly rhino *Coleodonta* and massive one-horned hairy *Elasmotherium*, perhaps no other feature so eloquently links the Sumatran rhino with its long and prosperous past.

RHINOCEROS IMMOBILIZATION AND CAPTURE

Rhinoceros Capture Beginnings

Before widespread application of chemical capture techniques, early African rhino capture operations used ropes and a chase vehicle. Although dangerous to the operator and stressful to the animal, some teams in East Africa became remarkably proficient at this form of capture (McCulloch and Achard, 1969). Chemical capture of rhinoceroses was first attempted with the dissociative anesthetic, phencyclidine, and the curariform muscle relaxant, gallamine triethiodide. In 1960 during Operation Noah, many black rhino (Diceros bicornis) were saved from the rising waters of the newly constructed Lake Kariba, bordering Zambia and Zimbabwe, using these novel techniques (Child and Fothergill, 1962; Harthoorn and Lock, 1960; King, 1965; Meadows, 1996). Phencyclidine and gallamine were succeeded by the easily reversible opioids (Condy, 1964), first morphine and dimethylthiambutene followed quickly by



Figure 48.2. The distinctive hair coat of a young Sumatran rhinoceros: a feature linking the primitive Dicerorhinus genus with its prehistoric past. (Image courtesy Dave Jenike, Cincinnati Zoo & Botanical Garden.)

the more potent opioids. Over the past 40 years, etorphine HCl (M99) has become the standard opioid for capture of the African and Asian rhinoceroses (Flamand, 1984; Henwood, 1989; Hitchens, 1972; Keep, 1969, 1973; King, 1965, 1969). Fentanyl citrate (Sublimaze), carfentanil citrate (Wildnil), and thiafentanil oxalate (A3080) are useful alternatives (De Vos, 1978; Hofmeyr, 1975). Pioneering investigation by early practitioners such as Toni Harthoorn, Eddie Young, Ian Hofmeyr, Ian Player, and many others provided the foundation on which future rhino chemical capture methods, including the present work, are based (Player, 1972; Harthoorn, 1973; Young, 1973).

Remote Drug Delivery: Equipment and Darting Techniques

An assortment of remote drug delivery equipment is available for rhinoceros capture, including new developments, yet some of the early systems are still in common practice today attesting to their simple and durable design. In captive and boma situations all darting systems can be used, but nylon darts (Daninject or Telinject with 60- mm \times 2-mm smooth needles) are preferred as they are quiet and relatively atraumatic. The authors prefer to hand-inject (using appropriate human protective safety measures) or pole-syringe captive rhinos, including animals held in bomas to eliminate the excitement phase associated with projectile darting.

For field capture of rhinoceroses on the ground or from a helicopter a robust and reliable darting method such as the Cap-Chur system is preferable. Dart barrels made of aluminum (Cap-Chur, Powder Springs, GA) or stainless steel (Deon Joubert, RSA) are the most reliable for field use, especially since power settings and impact energy are high, wind or downdrafts from the helicopter can be a problem, and the operator is often forced to shoot through vegetation. The dart needle should be 5 to 6 cm long for an adult rhino. Rhino skin can plug the lumen of a dart needle unless the needle has a relatively thick wall and narrow lumen (Cap-Chur NCL needles) or the tip is bent over (Fauncap dart needles) or the point is sealed and side ports are provided. The needle must have a bead, low barb or small collar about 25 mm from the base to hold the dart in the thick skin (Morkel, 1994).

Proper dart placement is essential to ensure good drug deposition. The dart should be placed perpendicular to the skin for deep intramuscular (IM) injection. (The thick skin of a rhino often makes an angled shot ineffective.) When darting from the helicopter, the muscles of the rump or the upper part of the hind leg offer the best target. In the boma or on foot, any large muscle mass can be used for dart placement although the neck and shoulder are preferable.

Recumbency and Positioning

Recumbency and positioning are critical considerations for safe anesthesia of rhinoceroses whether in a zoological setting or in the wild. Prior to induction in captivity, thick padding or heavy mats should be used to protect recumbent animals from the concrete floors common in these environments. Myositis and neuropathy are serious potential complications. Traditionally, rhinos immobilized in the field are maintained in or moved into sternal recumbency; however, irreversible muscle damage has developed in this position (especially if the rhino goes down on a slope facing upward with the full weight on its hind legs) as a result of occlusion of the blood supply to the limbs. Although uncommon, problems even occur with careful "placement" of the legs in an apparently natural position. With the rhino on its side, blood flow to the limbs is improved and circulation to the muscles allows delivery of oxygen and dissipation of carbon dioxide and heat generated while running. With the animal in lateral recumbency, the legs should be physically "pumped" up and down by hand every 20 minutes to aid circulation. We recommend that all black rhino that have undergone any degree of exertion be placed in lateral recumbency for at least a few minutes. The decision to move white rhinos onto their sides should be based on several factors including the degree of exertion, presence of muscle tremors, and duration of recumbency. White rhinos often experience significant muscle rigidity, paddling, and even convulsions under opioid anesthesia. These effects are exacerbated by lateral positioning but tend to resolve with time.

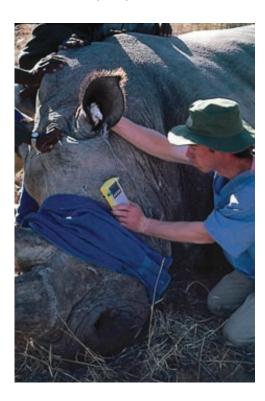


Figure 48.3. Anesthetic monitoring of free-ranging white rhinoceros (*Ceratotherium simum*). Note the use of a blindfold, cotton wool plugging ear canals and pulse oximeter attached to the pinnae.

Therefore, white rhinos should be positioned initially in sternal recumbency until complete relaxation is achieved (Kock, 1995).

Eyes and Ears The eyes of the recumbent rhino should be shielded with a large towel or appropriate-sized blindfold to prevent retinal damage from direct sunlight, dirt accumulation, and corneal abrasion from the environment (Figure 48.3). Foreign material should be washed from the eyes using physiological saline. The ear canals are plugged with cotton wool or a cloth while the rhino is anesthetized, leaving tabs for quick removal. Alternatively, when a large number of rhino are to be immobilized, connect two cloth-covered cotton wool plugs with cord so they remain together. If the rhino is being transported, its ears should remain blocked for the entire trip; however, the blindfold must be removed once the rhino is secure within the crate.

Anesthesia Monitoring

A thorough clinical examination with monitoring of vital functions (respiration, temperature, heart rate, capillary refill time) must be done regularly for the duration of anesthesia. Concentrate on respiration, temperature and heart rate, in that order. These functions are very much dependent on the degree of exertion and excitement before and during induction and must be kept in mind during your evaluation. Careful monitoring is especially important in old, debilitated, very

young, and heavily pregnant animals. Check if the entire dart contents were injected, especially if more than one dart was used, as the success of drug delivery may dictate protocols for anesthetic monitoring and antidote administration (Morkel, 1994).

Pulse oximetry provides an indirect measure of oxygen saturation of hemoglobin (SaO₂) and is valuable to help monitor blood oxygenation and pulse in anesthetized rhinoceroses (Figure 48.3). However, it should not be a replacement for thorough patient monitoring. Without simultaneous correlation with arterial blood gases, pulse oximetry is a tool best used to monitor trends in oxygen saturation rather than actual values. Based on lower oxygen affinity of white rhinoceros hemoglobin, it has been suggested that SaO₂ levels (ranging from lows of 40% up to 98%) (Kock, 1995; Atkinson, 2002) in rhinoceroses underestimate true oxygen saturation of hemoglobin when calculations are made using human formulae (Bush, 2004). The sensor clip is attached to the pinnae of the ear after removal of the epidermis by careful scraping with a serrated kitchen knife or on mucosal folds of the penis, vulva, or rectum. Place a cloth over the sensor, as ambient light affects the reading. In animals with excessive muscle rigidity or tremors, as is common in immobilized white rhinos, the sensor may fail to obtain an accurate reading. A rectal probe held against the nasal mucosa works well (must be applied beyond the pigmented area) and has also been used with varying success on the inner surface of the lips, against the gums, and in the rectum or vagina.

Respiration and Oxygen Respiratory depression is perhaps the most significant life-threatening complication encountered during routine anesthesia of rhinoceroses (Heard, 1992; Kock, 1995; Atkinson, 2002; Bush, 2004, 2005; Fahlman, 2004). Large recumbent animals experience cardiopulmonary depression and perfusion-ventilation disparities because of large size and abdominal organs impinging on the diaphragm. Severe respiratory compromise with hypoxemia, hypercapnia, and acidosis is more common with long captive procedures or under field conditions where higher doses of opioids are used to shorten induction times (Heard, 1992; Kock, 1995). Among the African species, these physiological changes are more prevalent in the white than black rhinoceroses (Bush, 2004, 2005).

Respiration is the first and most critical function to be monitored in rhinoceroses under anesthesia. In the field situation it is valuable to have a reliable person who does nothing but watch the respirations, noting rate and depth. Be sure there is a free flow of air in and out of the nostrils and that the blindfold does not restrict airflow. Concentrate on respiratory rate and depth by observing chest movement. When monitoring breaths on a bouncing vehicle, as with immobilized rhino transported on a sledge where it is difficult to watch chest movement, hook a finger in the nostril or hold your



Figure 48.4. Feeling for the warm expired air facilitates respiratory monitoring of an anesthetized juvenile white rhinoceros (Ceratotherium simum).

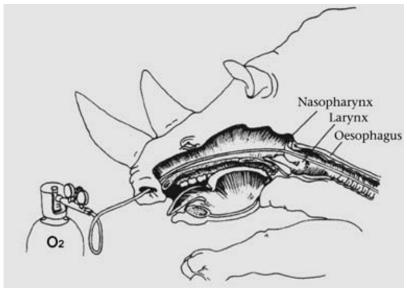
hand close to the nares to feel the warm exhaled air (Figure 48.4). Breathing must be deep and regular. Monitor respiration for at least 30 to 60 seconds to obtain an accurate picture of ventilatory pattern, as an immobilized rhino often gives two or three quick breaths followed by a period of apnea. Respiratory rate is approximately 10 to 15 breaths per minute on induction, going down to 4 to 8 bpm about 10 minutes post-induction when using potent opioids. Observation of venous blood color during venipuncture provides a reliable early indicator of blood oxygenation. Dark red, almost black blood indicates poor oxygenation, whereas a lighter red color is normal and correlates well with mucous membrane color (Morkel, 1994).

If a rhino stops breathing, give nalorphine HBr (Nalline), or consider complete reversal with naltrexone HCl (Trexonil). A painful stimulus often incites the apneic rhino to take a breath. Nalorphine given intravenously (IV) produces a marked and sustained improvement in the quality of respiration (Tables 48.2 and 48.3). Its use has been associated with an approximate 20% increase in the hemoglobin saturation of oxygen (SaO₂) based on pulse oximetry (Kock, 1995). Although widely reported to improve oxygenation (Rogers, 1993a,b), however, recent investigation suggests that nalorphine produces negligible change to oxygen partial pressures (PaO₂) in anesthetized rhinoceroses (Bush, 2004; Fahlman, personal communication). Since black rhino stand up readily with very small volumes of nalorphine, we recommend a dose of 5 mg nalorphine for adult black rhino and 25 to 30 mg for white rhino under field conditions. It is very safe to use nalorphine in white rhino, as this species rarely rises without stimulation, and even if arousal does occur adult animals are relatively harmless in a semi-narcotized state. IV doxapram HCl (Dopram; black rhino 200 mg, white rhino 400 mg) provides a smaller, transient improvement in respiratory rate and depth. Use doxapram with caution in white rhinos as it causes central nervous system excitation and exacerbates muscle tremors; effects are best noted if used in conjunction with nalorphine and supplemental oxygen.

Nasal or tracheal insufflation of oxygen (O₂; 15–30 L/ minute) can produce a rapid and significant increase in blood oxygen saturation in immobilized rhinoceroses. Although it did not correct systemic acidosis or hypercapnia, O2 insufflation substantially improved oxygenation and anesthetic safety (Bush, 2004; Fahlman, 2004). A variety of factors influence pulmonary blood gas exchange, including dose of anesthetic drug, position of the rhino during immobilization, body temperature, oxygen delivery, and size of the animal. Oxygen supplementation at the flow rates commonly used for rhinoceroses appears to produce a more profound improvement of patient oxygenation (PaO₂ 108-194 mmHg) in subadult African rhinos compared to adults, perhaps indicating greater ventilation-perfusion mismatch with larger body size (Fahlman, 2004, unpublished data).

A control valve and flow meter are attached to the O₂ bottle and oxygen is administered via a flexible silicon or rubber nasogastric tube (smooth and round edges to prevent damage to nasal mucosa), measuring 2 m long and 9 to 14 mm inside diameter (Figure 48.5). Concurrent monitoring of the respiratory rate and depth, and blood oxygenation remains essential. A low dose of nalorphine increases the rate and depth of respiration and improves the efficacy of oxygen supplementation. Oxygen supplementation is one of the few practical solutions to enhance pulmonary gas exchange in immobilized rhinoceroses and if used wisely one bottle is sufficient for many animals. Therefore, we recommend immediate intranasal or tracheal insufflation of oxygen in all recumbent rhinoceroses. Within a few minutes vital statistics provide information about respiratory function and in most situations all physiological parameters are satisfactory. A small percentage of animals, however, develop a physiological crisis in which oxygen supplementation is critical. Aluminum oxygen bottles are now available that are small and lightweight, making them convenient for helicopter use.

Body Temperature Body temperature is an important parameter and the best indicator of the degree of exertion endured by the rhinoceros before induction. Keep in mind that for every 1° increase in body temperature above normal, there is a marked increase in oxygen consumption. A rhino's body temperature varies slightly during the day as the ambient temperature changes. Black rhino immobilized without excessive exertion have a rectal temperature of between 36°C and 39°C. Young rhino tend to have a higher body temperature than adult rhino after running a comparable distance. An animal with a body temperature of greater than 39°C must be liberally soaked with cool water. Although



Source: Bush, M.R., Raath, J.P., Grobler, D. and L. Klein. 2004. Severe hypexaemia in field-anaesthetised white rhinoceros (Cerustotherium simum) and effects of using tracheal insufflation of oxygen. J. S. Afr. Vet. Assoc. 75(2): 79-84.

Figure 48.5. Illustration of the nasogastric tube tracheal insufflation technique for oxygen delivery in a recumbent white rhinoceros (Ceratotherium simum) under field conditions. (Adapted from Bush MR, Raath JP, Grobler D, et al. Severe hypoxaemia in field-anaesthetised white rhinoceros (Ceratotherium simum) and effects of using tracheal insufflation of oxygen. J South Afr Vet Assoc 2004;75:79–84. (Illustration courtesy the South African Veterinary Association.)

drenching with water is important, it does not have a dramatic effect in lowering the body temperature, as there is considerable thermal inertia in such a large mammal. It helps to fan the rhino with branches or cloths after the animal has been wetted with water. Holding leafy branches over the rhino to provide shade can help lower the temperature, but it is important that people do not crowd around an immobilized rhino and prevent air movement. A rhino with a body temperature over 39°C must be processed quickly, whereas a temperature of greater than 41°C mandates immediate delivery of the antidote.

Pulse and Blood Pressure Heart rate is best obtained using a stethoscope, whereas the pulse is readily palpable under the base of the tail (caudal artery) or on the inside of the ear (medial auricular artery). Subjectively evaluate pulse quality and compare with the pulse oximeter reading. It is often quite easy to visualize heart compressions by watching the chest wall or by feel with a hand placed over the cardiac window. The heart rate is usually 55 to 80 beats per minute (bpm), although it is higher in rhino that have undergone marked exertion, especially young animals (as much as 140 bpm). Cardiovascular function and peripheral perfusion are assessed by capillary refill time (CRT) and is measured by blanching the rhino's gum for several seconds and then releasing. The observed delay or refill time should not exceed 2 seconds (Morkel, 1994).

Hypertension is prevalent under etorphine anesthesia in black and white rhinoceroses (LeBlanc, 1987;

Heard, 1992; Hattingh, 1994). One report in white rhino anesthetized under field conditions noted an apparent reduction in blood pressures when azaperone tartrate (Stressnil) replaced fentanyl in etorphine-based combinations, an effect observed despite the higher dose of etorphine used in the cocktails containing azaperone (Hattingh, 1994). These conclusions, however, appear dubious as fentanyl is itself a potent opioid with prominent hypertensive effects; possessing an activity approximately 1/15 that of etorphine, fentanyl was likely a confounding factor in the study. Although no definitive mechanism has been identified, increased sympathetic nervous system action, peripheral vasoconstriction, and hypoxemia are proposed factors in etorphine-induced hypertension in both rhinos and equids (Daniel and Ling, 1972; Heard, 1992). Opioid related hypoxemia might induce sympathetic system stimulation and hypertension; once hypoxia resolves the sympathetic response and associated hypertension disappear.

RHINOCEROS ANESTHESIA IN CAPTIVITY

Guidelines for Anesthesia of Captive Rhinoceroses

The large size of the rhinoceros belies an unexpected sensitivity to the opioid class of pharmacological agents (Raath, 1999). Surprisingly, the same dose of carfentanil citrate used to immobilize a 20-kg blackbuck (*Antelope cervicapra*) would also fully immobilize a 2,200-kg white rhinoceros (*Ceratotherium simum*), making the rhino over 100 times more opioid sensitive per unit mass than

the average artiodactylid. This inordinate sensitivity of the rhinoceros family to the opioid class—although responsible for the undesirable changes observed in cardiopulmonary function—also makes it possible to adapt less potent mixed agonist-antagonist opioid agents into anesthetic protocols for both captive and wild rhinoceroses (Radcliffe, 2000a; Walzer, 2000; Bush, 2005).

Planning for anesthetic events should include preparation of the subject and environment in which these variables can be controlled. Depending on the purpose for anesthesia it is generally desirable to fast the animal for 12 to 48 hours prior to anesthesia (Radcliffe, 2000b). However, fasting is certainly not essential, as evidenced by the many successful field operations in which capture of wild rhinoceroses is conducted in the absence of pre-anesthetic fasting. Water access should be denied for at least 12 hours and all water sources removed from the environment prior to drug delivery, as regurgitation has been noted in white rhinoceroses (Raath, 1999). Both passive and active regurgitation of stomach contents are known. The latter are very rare but quite spectacular. Passive regurgitation is common in immobilized rhinos, presumably secondary to drug- or hypoxemia-induced relaxation of the cardiac sphincter. Because of the risks of regurgitation and inhalation pneumonia, great care must be taken with positioning of the head and nostrils, especially with animals in lateral recumbency.

Habitual patterns of behavior are important aspects of captive rhinoceros husbandry, facilitating close medical management. Anesthesia techniques should be adapted as part of these conditioning protocols. Regular visits by animal health staff to rhino barns or bomas for acclimatization to the sights, sounds, and smells of the veterinary profession help limit the stress of such procedures. In boma situations it is helpful to learn the nature of each animal, including its likes and dislikes while also listening carefully to the keeper in charge of caring for the animal.

African Rhinoceros Captive Anesthetic Regimens

White Rhinoceros (Ceratotherium simum) The adult white rhinoceros is large and generally placid in captivity. Anesthesia with potent opioids is often associated with marked hypermetria, muscle rigidity, trembling, head shaking, and limb paddling (Figure 48.6). These effects are undesirable and can be prevented by preanesthetic administration of the sedative or tranquilizer component of the cocktail. In captive animals, initial dosing with IM azaperone 20 to 30 minutes prior to induction with etorphine helps preclude muscle spasms and rigidity. With wild rhinos, positioning in sternal recumbency until complete relaxation is achieved was deemed important in field practice (Kock, 1995). New techniques offer alternatives for long or painful procedures by incorporation of the highly specific α_2 agonist medetomidine HCl (Domitor) into routine



Figure 48.6. Typical induction posture in adult white rhinoceros (Ceratotherium simum) under the effects of etorphine, illustrating characteristic head elevation, raised hackney action of forelimbs, and muscle rigidity. (Image courtesy Rolfe Radcliffe, Living Fossil Productions.)

rhino immobilization protocols (Citino, personal communication).

Mixtures of etorphine or carfentanil combined with a sedative are standard agents for anesthesia of the captive white rhinoceros (Table 48.1). Doses ranging from 0.8 mg to 3 mg of etorphine and 1.2 mg carfentanil are common, with supplemental opioids given IM or IV to extend anesthesia (Heard, 1992; Walzer, 2000). Following immobilizing doses of etorphine or carfentanil, other agents provide additional muscle relaxation and a deeper plane of anesthesia, including IV propofol, guaifenesin, ketamine, midazolam, and α_2 -agents (Klein, 1997; Zuba and Burns, 1998; Walzer, 2000; Kock, 2006). Muscle relaxation is critical for deep ventilation and to counteract the associated risk of oxygen depletion from muscle tremors and hyperthermia inherent with use of potent opioids. Lower opioid doses are indicated in zoo-conditioned animals, yet the potent opioids are still associated with significant cardiopulmonary changes, especially as procedure length increases (Heard, 1992). One captive white rhinoceros immobilized with etorphine remained hypoxemic despite maintenance of inhalation anesthesia using intermittent partial pressure ventilation (Cornick-Seahorn, 1995). Hypertension is common, whereas hypoventilation, pulmonary shunting, and atelectasis induce hypoxia and hypercapnia (Heard, 1992; Bush, 2004).

Butorphanol tartrate (Torbugesic) combinations are replacing use of more potent opioids for rhinoceros anesthesia in many zoological settings as safe and reliable anesthetic planes can be achieved for most procedures, including surgery (Radcliffe, 2000a,b,c). Although not appropriate for all applications (i.e., fractious, nonconditioned animals or those with access to large areas) butorphanol combinations are highly effective. The author has used a mixture of butorphanol and azaperone

Table 48.1. Suggested doses for chemical restraint of adult captive rhinoceros producing anesthetic planes from sedation to recumbency.

Rhino Species	Standing Sedation Protocol	Reversal	Reference Comments	Recumbency Protocol	Reversal	Reference Comments
White rhinoceros	50–70 mg Butorphanol (BT) + 100 mg Azaperone IM hand-injection plus constant rate infusion (CRI)	Naltrexone at 2.5 mg per mg BT 1/2IV 1/2IM	Radcliffe, 2000a, 2000b; use CRI in long procedures	70–120 mg Butorphanol + 100–160 mg Azaperone IM hand injection	Naltrexone at 2.5 mg per mg BT 1/2IV 1/2IM	Radcliffe, 2000a; supplemental IV dosing or CRI
	120–150 mg Butorphanol + 5–7 mg Medetomidine (MED) IM dart (Give 1–2 mg Nalorphine IV to keep standing)	Naltrexone at 1 mg per mg BT Atipamezole at 5 mg per mg MED	Citino, unpubl. data	120–150 mg Butorphanol + 5–7 mg Medetomidine (IM dart; recumbency ~20 minutes)	Naltrexone at 1 mg per mg BT Ati- pamezole at 5 mg per mg MED	Citino, unpubl. data; improved analgesia for surgery
	0.8–1.5 mg Etorphine (M99) IM dart	Naltrexone at 40 mg per mg M99	Portas, 2004	2–3 mg Etorphine + 20–40 mg Azaperone IM dart 1.2 mg Carfentanil IM dart	Naltrexone at 40 mg per mg M99 Naltrexone at 100 mg per mg M99	Portas, 2004 Portas, 2004
Black rhinoceros	25–50 mg Butorphanol IV or IM hand injection	Naltrexone at 2.5 mg per mg BT 1/2IV 1/2IM	Radcliffe, 2000c and unpubl. data; use for sub-adults and crating	1–1.5 mg Etorphine + 100 mg Azaperone IM hand injection	Naltrexone at 50 mg per mg M99 1/2IV 1/2IM	Radcliffe, unpubl. data; lower M99 doses with hand injection
	1.5–2 mg Etorphine + 2–3 mg Medetomidine (Give 1–2 mg Nalorphine IV to keep standing) IM dart	Naltrexone at 30 mg per mg M99 Atipamezole at 5 mg per mg MED	Citino, unpubl. data	1.5–2 mg Etorphine + 2–3 mg Medetomidine (IM dart; recumbency ~15 minutes)	Naltrexone at 30 mg per mg M99 Atipamezole at 5 mg per mg MED	Citino, unpubl. data; enhanced analgesia for dental surgery
	2–2.5 mg Etorphine + 10 mg Detomidine (DET) + 15 mg Butorphanol IM dart	Naltrexone at 40 mg per mg M99 Atipamezole at 5 mg per mg DET	Portas, 2004	2.5–3 mg Etorphine + 60 mg Azaperone IM dart	Naltrexone at 20–40 mg per mg M99	Portas, 2004
Greater one-horned rhinoceros	100 mg Butorphanol + 100 mg Azaperone IM hand injection	Naltrexone at 2.5 mg per mg BT 1/2IV 1/2IM	Radcliffe and Lung, unpubl. data	3.5–3.8 mg Etorphine + 14 mg Detomidine + 400 mg Ketamine IM pole syringe	150–300 mg Naltrexone 1/2IV 1/2IM No reversal DET	Atkinson, 2002
Sumatran rhinoceros	25–40 mg Butorphanol IM hand injection	Same	Radcliffe, 2002; use Azaperone in longer procedures	30–50 mg Butorphanol + 50–60 mg Azaperone IM hand injection 1 mg Etorphine + 60 mg Azaperone IM hand injection	Naltrexone at 2.5 mg per mg BT 1/2IV 1/2IM Naltrexone at 50 mg per mg M99 1/2IV 1/2IM	Radcliffe, 2002; higher doses for recumbency Radcliffe, unpubl. data; Azaperone 20 min. < M99 or suppl. Midazolam

From Citino, unpublished data; Radcliffe, unpublished data; Atkinson MW, Bruce H, Gandolf AR, et al. Repeated chemical immobilization of a captive greater one-horned rhinoceros (*Rhinoceros unicornis*), using combinations of etorphine, detomidine, and ketamine. *J Zoo Wildl Med* 2002;33:157–162; Portas TJ. A review of drugs and techniques used for sedation and anaesthesia in captive rhinoceros species. *Aust Vet J* 2004;82:542–549.

for standing sedation and recumbent anesthesia in all four rhinoceros species maintained in captivity (white, black, greater one-horned, and Sumatran) with safe, predictable results (Radcliffe, 2000a,c, unpublished data). Butorphanol doses for white rhino range from 50 to 120 mg for an adult and 10 to 20 mg for a calf or juvenile animal, whereas azaperone doses range from 100 to 160 mg for an adult with supplemental doses given up to a maximum of 300 mg (Tables 48.1 and 48.4). IV butorphanol supplementation is highly effective at inducing recumbency in white rhinos after initial drug delivery, if needed and desirable. IV azaperone has been associated with adverse extrapyramidal reactions in the horse and white rhino and should be avoided (Radcliffe, 2000a).

Black Rhinoceros (Diceros bicornis) Black rhino appear predisposed to excitation during induction with etorphine, especially with remote drug delivery in zoological environments (Portas, 2004). Using appropriate human safety practices, the stress of darting can be avoided by hand injection, thereby alleviating much of the undesirable excitatory phase black rhinos experience while also significantly reducing the total dose of opioid agents required (Radcliffe, unpublished data; Table 48.1). In bomas, to limit the "undesirable excitatory phase" great care should be taken to minimize the number of people and unusual objects close to the boma. Noise and movement should be avoided and once recumbent the rhino's eyes should be covered and ears blocked as soon as possible. Significant induction risks include lacerations, limb and foot injuries, head trauma, damage to nasal sinuses, horn avulsion, and even death. With careful animal conditioning and procedure planning the risks of induction excitation are easily minimized. Likewise, antagonism of narcotic anesthesia in the black rhino is characterized by rapid and aggressive recoveries mandating extra care; never stand in front of a narcotized rhino, as arousal is often sudden and unpredictable (Kock, 2006).

As in the other rhinoceros species, potent opioids (primarily etorphine) have historically been used for anesthesia of captive black rhinoceroses with predictable results (Portas, 2004). Zoo conditioned animals require much lower doses of etorphine (1-1.5 mg) than their wild counterparts, especially when administered by hand injection or pole syringe (Table 48.1). Butorphanol alone or in combination with azaperone or detomidine HCl (Dormosedan) has also been used in the black rhino, although its use is primarily limited to subadult animals, crating and translocation procedures or well-conditioned animals, because black rhino are easily excitable and may override drug effects (Radcliffe, 2000c, unpublished data). If butorphanol is chosen as the primary opioid agent, expect light planes of anesthesia and the need for frequent redosing. A more thorough discussion of mixed agonist-antagonist opioid cocktails and newer α_2 -agents for use in both captive and field immobilization protocols for the African rhinoceros can be found in the New Techniques section of this chapter and Tables 48.1 and 48.2.

Asian Rhinoceros Captive Anesthetic Regimens

Indian or Greater One-Horned Rhinoceros (Rhinoceros *unicornis*) Despite the common occurrence of Indian rhinos in zoological parks and a propensity for foot problems necessitating chronic care, few published accounts of anesthesia in captive greater one-horned rhinoceroses exist (Atkinson, 2002; Portas, 2004). One report combined injectable and inhalation anesthesia in a female Rhinoceros unicornis for ovariohysterectomy using etorphine and isoflurane in oxygen. The 7-hourlong anesthesia (much of it in dorsal recumbency) was considered effective despite the animal succumbing to post-surgical complications (Klein, 1997). The most complete summary of captive anesthesia in this species, however, describes serial opioid-based anesthesia to facilitate long-term medical foot care in one animal. A combination of etorphine-detomidine (3-3.6 mg and 10-14 mg IM, respectively) was given by projectile dart or etorphine-detomidine-ketamine (3.5–3.8 mg, 14 mg and 400 mg IM, respectively) administered by polesyringe (Atkinson, 2002). Use of the pole-syringe for drug delivery was preferred, because darting was limited by a small target area among the peculiar anatomic neck folds and by drug selection for small dart volumes. Although both drug combinations proved efficacious, subjective assessment suggested that the etorphinedetomidine-ketamine protocol produced more rapid induction, lowered the need for supplemental ketamine, and shortened reversal times (Atkinson, 2002).

The author has used butorphanol and azaperone (100 mg of each drug mixed in a syringe and given by hand injection) to induce standing sedation in the Indian rhinoceros (Radcliffe and Lung, unpublished data). A combination of butorphanol and detomidine (120 and 80 mg, respectively) produced sternal recumbency for surgical repair of a rectal prolapse (Bertelsen, 2004). As in the white rhinoceros, these protocols provide adequate muscle relaxation, sedation, and analgesia while being completely reversible with the pure opioid antagonists naltrexone or naloxone hydrochloride (Narcan). Naltrexone is preferred unless short immobilization intervals are anticipated since renarcotization is common using naloxone alone; naloxone provides complete reversal for a short duration (approximately 30-60 minutes) and is only suggested if repeat procedures are planned for the same day (Gandolf, 2000; Radcliffe, 2000a; Bertelsen, 2004; Portas, 2004).

Javan or Lesser One-Horned Rhinoceros (*Rhinoceros* sondaicus) *Rhinoceros sondaicus* is the only rhino not presently represented by captive specimens and was only extraordinarily displayed in zoological gardens

during the seventeenth, eighteenth, and nineteenth centuries (Rookmaaker, 1998). Although historical records indicate that at least 22 Javan rhino were captured between 1647 and 1939, only four survived long enough to reach zoo exhibits in Adelaide, Calcutta, and London (Rookmaaker, 1998). The entire surviving wild population of Javan rhinoceroses can be found in Ujong Kulon National Park in West Java (*n* approx 50) and Cat Tein National Park in Vietnam (*n* approx five). No accounts of Javan rhinoceros anesthesia exist, but techniques presumably would be analogous to approaches used for the Sumatran rhinoceros (*Dicerorhinus sumatrensis*) or greater Asian one-horned rhinoceros (*Rhinoceros unicornis*), with size difference being a notable exception.

Sumatran Rhinoceros (Dicerorhinus sumatrensis) Few reports of Sumatran rhinoceros anesthesia exist because captive specimens are rare. Etorphine (0.98-1.23 mg or 1 mg) combined with acepromazine (PromAce; 4–5 mg) or azaperone (60 mg) has been used to anesthetize captive Sumatran rhinos (Portas, 2004; Radcliffe, unpublished data). As with the African species, muscle rigidity and cardiopulmonary depression are common with use of these potent opioid agents and pre-anesthetic administration of a tranquilizer is prudent to limit muscle tremors and improve respiratory function. Total azaperone doses should be kept to 100 mg or less, as ataxia has been noted upon recovery with higher doses in this species. Butorphanol has been combined with detomidine for standing sedation (Citino and Morris, personal communication), whereas the author routinely uses a mixture of butorphanol and azaperone for standing sedation and full recumbent procedures (Table 48.1) (Radcliffe, 2002).

As with the African species, butorphanol combinations are preferred in captive Sumatran rhinoceroses to preclude the adverse cardiopulmonary changes associated with use of more potent opioids. For adult animals, butorphanol at a dose of 60 to 80 µg/kg with azaperone at 80 to 100 µg/kg and a range of 30 to 50 mg and 50 to 60 mg butorphanol and azaperone, respectively, is recommended, with higher butorphanol doses being used on occasion to produce recumbency. Antagonism of the butorphanol effects is accomplished with naltrexone at a dose of 2.5 times the induction dose of butorphanol (Table 48.1) (Radcliffe, 2002). Other tranquilizers may be used in place of azaperone such as the α_2 -agonists, but care should be exercised as hypoxemia has been reported with use of these sedatives. Local anesthetics may facilitate invasive procedures; however, use of more potent narcotics such as etorphine or other pharmacological agents such as ketamine may be indicated to induce surgical anesthesia.

New Captive Anesthesia Techniques

Although much has been learned about rhinoceros anesthesia, limitations still hinder safe and reliable

procedures for these large mammals, especially where prolonged recumbency or surgery is required (Heard, 1992; Klein, 1997). Standing restraint where possible using mixed agonist-antagonists shows promise (Radcliffe, 2000a,b). For the black rhinoceros, in which potent opioids are still often preferred over mixed agonists, challenges include marked respiratory depression, inadequate muscle relaxation, need for frequent re-dosing, and incomplete analgesia in painful procedures. An exciting new development in captive anesthesia of African rhinoceroses incorporates the potent α_2 -agonist medetomidine with etorphine or butorphanol (Citino, unpublished data). Because α_2 -agonists exacerbate respiratory depression and hypotension, contribute to dehydration, and alter thermoregulatory mechanisms, they must be used with caution in rhinos of unknown health status, especially old and debilitated animals. However, under captive conditions in which the health of an animal is known and a specific type of anesthesia is desirable, α_2 agents are effective supplements.

For the black rhino, medetomidine (2-3 mg representing 2-2.9 µg/kg IM dose; 20 mg/ml solution) is combined with etorphine (1.5-2 mg representing 1.5–1.7 μg/kg IM dose) (Citino, unpublished data) and given by dart. The investigators were able to begin safe animal manipulations at approximately 9 minutes, with full recumbency achieved in 15 minutes. This combination facilitated very painful procedures, including molar extractions and foot surgery, with the additional supplement of an IV guaifenesin-ketamine drip (1 g ketamine in 1 L 5% GGE solution) to enhance peripheral analgesia. Relaxation was excellent with easy access to the oral cavity for dental surgery. Physiological parameters were considered normal with concomitant nasal oxygen insufflation. Recovery from anesthesia was smooth and rapid, with no evidence of resedation or renarcotization using naltrexone at 30 mg per mg etorphine and atipamezole HCl (Antisedan) at 5 mg per mg medetomidine.

For white rhino, in which but orphanol has proved so effective in captive settings, the same investigator is using medetomidine (5-7 mg IM) and butorphanol (120-150 mg IM) to provide enhanced muscle relaxation and analgesia properties (Citino, unpublished data). The animals can be manipulated within approximately 11 minutes of IM drug delivery, with full recumbency in 20 minutes. The addition of medetomidine into these protocols has significantly improved analgesia properties for such painful ophthalmic procedures as eye enucleation and conjunctival flap surgery. As with the black rhinoceros, a 5% guaifenesin-ketamine drip was deemed useful for long procedures and to enhance peripheral analgesia. Antagonism was complete using naltrexone at 1 mg per mg butorphanol and atipamezole at 5 mg per mg medetomidine (Citino, unpublished data).

RHINOCEROS ANESTHESIA IN THE WILD

Guidelines for Anesthesia of Wild Rhinoceroses Field anesthesia of Asian and African rhinoceroses is often undertaken to facilitate urgent conservation actions such as dehorning, ear-notching, microchip application, radio-collaring, and horn transmitter implantation or translocation to safe areas (Dinerstein, 1990; Kock, 1990, 1995). Ideally rhino capture operations should be conducted when temperatures are lower than 25°C, usually in the early morning or late afternoon. Darting free-ranging rhino when ambient temperatures are high increases the risk of elevated body temperatures and associated physiological stress. If working in the late afternoon, do not dart a rhino unless there is enough daylight remaining (leave an hour or more to process the animal and deal with potential problems) (Rogers, 1993a,b). If a rhino has run hard enough for its skin to become dark with sweat, the rhino's body temperature often exceeds 39°C. Such an animal should not be darted or if it has already been darted, it must be drenched with water and processed quickly. If the temperature of an immobilized rhino rises above 41°C, give the antidote and release the animal immediately.

With good dart placement, recumbency should follow within 3 to 6 minutes post-drug delivery (Morkel, 1989; Kock, 2006). Induction is usually quicker in young rhino and longer in large bulls and heavily pregnant cows. If there are no signs at about 6 minutes, the rhino should be darted again. Induction times of less than 3 minutes may indicate an overdose and it is important to get to such an animal quickly so that the respiration and other vital functions can be monitored and oxygen, nalorphine or doxapram given, if necessary. In protocols incorporating thiafentanil, rapid inductions are expected and less of a concern. IV opioid use should be avoided because of risks of apnea; however, if necessary give the opioid slowly while keeping a close eye on respiration. For the same reason caution must be exercised when giving midazolam or α_2 -agonists by the IV route.

As a rhino becomes affected by etorphine, its pace shortens, the forelegs are lifted higher in a classic "Hackney gait," and the head is elevated (Figure 48.6). The rhino then starts to blunder through bushes and slows down before going into lateral or sternal recumbency. In rough terrain rhino have a tendency to run downhill once they are heavily narcotized and may easily injure themselves by running into a gully or water source. With a quick induction, rhino tend to go down in sternal recumbency. Occasionally the forelegs collapse first and the hindquarters remain elevated. In this situation the full weight of the abdominal organs press on the diaphragm and respiration can be severely compromised, especially in heavily pregnant females, in which the weight of the fetus adds additional pressure. Such animals must be immediately pushed onto their side. Usually a rhino is fully recumbent on arrival;

however, if it is still on its feet the brake rope can be placed around one of its rear legs, the blindfold over its eyes, and cotton wool in its ears. On arrival at an immobilized rhino make a quick estimate of its age and body condition. Older or debilitated rhino need special care. Be sure that nothing impedes respiration or is pushing against the rhino's belly, chest, or nostrils. Also be sure the rhino is not facing downhill with pressure against the diaphragm. Field personnel must work quickly, whereas the rhino is recumbent and it helps to prepare a prioritized checklist before beginning each rhino capture (see Practical Strategies for Rhinoceros Field Anesthesia).

African Rhinoceros Wild Anesthetic Regimens White Rhinoceros (Ceratotherium simum) With the high doses of opioids used to speed induction under field conditions, the safe anesthesia of wild white rhinos represents one of the most challenging branches of rhinoceros anesthesia (Table 48.2). Hypoxia, hypercapnia, hypertension, tachycardia, and acidosis are common physiological abnormalities reported in anesthetized white rhino (Heard, 1992; Bush, 2004). Numerous techniques have been developed to help alleviate the significant opioid-induced cardiopulmonary depression in African rhinos. These include use of partial agonistantagonist agents such as nalorphine to reverse the μ-regulated opioid respiratory depression, respiratory stimulants such as doxapram, nasal or tracheal insufflation of oxygen, and incorporation of mixed agonistantagonist agents into more potent opioid-based protocols to influence receptor effects (Kock, 1995; Radcliffe, 2000a; Bush, 2004, 2005; Fahlman, 2004).

Opioid doses for field anesthesia of adult white rhinoceroses range from 3 to 4.5 mg of etorphine plus 40 to 60 mg azaperone or 10 to 20 mg detomidine (Table 48.2) (Rogers, 1993a; Kock, 1995; Bush, 2004). Hyaluronidase (Hylase; 5,000 IU) is often incorporated into darting protocols for rhinoceroses to shorten induction time (Morkel, 1989). With hyaluronidase white rhinos stopped moving 2 to 3 minutes sooner but often remained standing (Kock, 1995). Fentanyl has been incorporated into drug cocktails for white rhinoceroses but is rarely used today. The rule of thumb for replacing the opioid component mixes etorphine and fentanyl at the following ratio: one-third etorphine with two-thirds equivalent dose of fentanyl (1 mg of etorphine is equipotent to 15 mg of fentanyl) (Rogers, 1993a). Historically, the parasympatholytic agent, hyoscine, was combined with opioids to induce pupillary dilation and "temporary blindness" to ease handling (Player, 1972; Rogers, 1993a); however, its use is no longer widely accepted because of undesirable side effects and is now considered obsolete (Kock, 1995; Raath, 1999).

An extensive study of white rhinoceros anesthesia incorporating several drug protocols and 141 immobilizations over a 2-year period was conducted in

Table 48.2. Suggested doses for chemical restraint of adult wild rhinoceros including supplemental agents used for respiratory support.

		Immobilization		Respiratory Su	ıpport
Rhino Species	Protocol	Reversal	Reference Comments	Protocol	Reference Comments
White rhinoceros	2–3.5 mg etorphine (M99) + 40–90 mg butorphanol (BT) + 25–50 mg midazolam (MDZ) + IM dart	Naltrexone at 40 mg per mg M99 IV (full reversal) OR 2–2.5 mg diprenorphine (M50:50) per mg M99 IV (reverses M99, but not BT)	Bush, 2005; NEW technique reduces respiratory depression, hypoxia, muscle rigidity and tremors, but with relatively long induction times	Produces immobile rhino in ~10 minutes and crating WITHOUT partial opioid reversal In case of inadvertent overdose or cardiopulmonary suppression give Diprenorphine to reverse the M99 while preserving the sedative effects of the BT	Bush, pers. com. and unpubl. data; reverse part or all of opioid effects based on desired outcome
	3-4.5 mg etorphine + 100-250 mg azaperone (40-60 mg if crating) (replace azaperone with 10-20 mg detomidine if no transport) IM dart	For crate reversal: 6-12 mg (2-3 × M99 dose IV) M50:50 plus 1-2 mg naltrexone IV if pushing	Kock, 1995, 2006; Rogers, 1993a; still considered standard translocation protocol	ALL WHITE RHINO: Mandatory 1 mg M50:50 plus 10 mg nalorphine IV OR 20–30 mg nalorphine IV OR	Kock, 1995, 2006; Morkel, unpubl. data
	Consider 5–20 mg midazolam slowly IV for muscle relaxation	For field/boma reversal: naltrexone at 40 mg per mg M99 IV (full reversal)	Morkel, unpubl. data Kock, 1995	20–40 mg nalbuphine IV	
Black rhinoceros	4 mg etorphine + 40-60 mg azaperone (replace azaperone with 100 mg xylazine or 10 mg detomidine) + 5000 IU hyaluronidase IM dart	For crate reversal: 10–20 mg nalorphine per mg M99 plus 1–2 mg M50: 50 IV For field/boma reversal: naltrexone at 40 mg per mg M99 IV (full reversal)	Morkel, 1989; Higher M99 doses for Diceros bicornis bicornis Kock, 1992, 2006; hyaluronidase is always recommended	NOTE: DO NOT use the white rhino respiratory protocol in black rhino as it will cause arousal INSTEAD: 5 mg nalorphine IV; titrate to effect IMPORTANT to have animal lateral and "pump" legs every	Morkel, unpubl. data Kock, 2006
	2–2.5 mg thiafentanil (A3080) + 2–2.5 mg etorphine IM dart	Same	Rogers, 1993b	20 minutes	
Greater one-horned rhinoceros	2–2.5 mg etorphine iM dart 2–2.5 mg etorphine + 10 mg acepromazine IM dart OR 0.7 mg carfentanil (CF)	Diprenorphine at 2.5 mg per mg M99 IV Naltrexone at 100 mg per mg carfentanil IV	Dinerstein, 1990; One sudden arousal noted; Induction times longer for breeding males	Cardiopulmonary depression not reported; 6–10 breaths per min Surround target rhino with 10–15 trained elephants	Dinerstein, 1990
Sumatran rhinoceros	2 mg etorphine + 80 mg azaperone + 5000 IU hyaluronidase IM dart OR Use M99: BT: MDZ 80 mg butorphanol +	Naltrexone at 50 mg per mg M99 1/2IV 1/2IM	Author suggestion (extrapolated from captive animals)	Treat like black rhino; muscle rigidity and tremors common Use 5 mg midazolam to relax Use 5 mg nalorphine for partial reversal of respiratory depression	Radcliffe, 2002 and unpubl. data
	80 mg azaperone IM dart	Naltrexone at 2.5 mg per mg BT 1/2IV 1/2IM	Use for compromised animal in snare	If rhino is approachable give 25–40 mg butorphanol IV rather than via dart	Radcliffe, 2002 and unpubl. data

From Bush, Citino, Grobler, unpublished data; Morkel, unpublished data; Radcliffe, unpublished data; Kock MD, Meltzer D, Burroughs R, eds. *Chemical and Physical Restraint of Wild Animals: A Training and Field Manual for African Species*. Harare, Zimbabwe: Zimbabwe Veterinary Association Wildlife Group and International Wildlife Veterinary Services, 2006; Rogers PS. 1993a. Chemical capture of the white rhinoceros (*Ceratotherium simum*) OR 1993b. Chemical capture of the black rhinoceros (*Diceros bicornis*). In: McKenzie AA, ed. *The Capture and Care Manual*. Pretoria, South Africa: Wildlife Decision Support Service and South African Veterinary Foundation.

Zimbabwe to enable dehorning operations (Kock, 1995). Initial immobilization mortality was quite high at 7% and was primarily attributed to hypoxemia and cardiovascular collapse. Subsequent captures used lower opioid immobilizing doses and simultaneously incorporated routine use of nalorphine (10-20 mg) or nalbuphine HCl (Nubain; 20-40 mg) to help improve respiration, especially in longer procedures in which mortality was most prevalent. Of the various drug combinations tested (etorphine alone and in combination with fentanyl, xylazine, or detomidine), the etorphinedetomidine combination was considered superior because it was empirically judged as smoother and more rapid (no statistical significance). Pulse rates and creatinine phosphokinase (CPK) levels were significantly lower with the etorphine-detomidine combination, suggesting improved cardiac function and less muscle damage, respectively (Kock, 1995). Good muscle relaxation was observed without the rigidity and paddling common with use of potent opioids in the white rhino. The ratio of etorphine to tranquilizer was critical and dose dependent, likely reflecting differences in drug pharmacology and onset of action.

An effective alternative for mitigating muscle rigidity in wild white rhinos is use of midazolam (Morkel, unpublished data) (Table 48.2). Since immobilized white rhinoceroses are often first encountered in a standing position with a rigid body stance (Figure 48.6), IV midazolam at 5 to 20 mg is effective in inducing good muscle relaxation and recumbency. The Zimbabwe workers noted that even small incremental increases in etorphine in the initial immobilizing dose or re-dosing with etorphine resulted in poorer muscle relaxation and increased head shaking, jerking, and limb paddling (Kock, 1995). Midazolam has excellent muscle relaxation properties and is a useful adjunct in these situations.

Black Rhinoceros (Diceros bicornis) Capture related stress appears to be a significant factor in field immobilization of the black rhinoceros resulting in morbidity and mortality in the post-capture period. Rapid immobilization using high opioid doses in combination with hyaluronidase is the single most critical factor in reducing stress during black rhino capture (Morkel, 1989; Kock, 1992). Furthermore, higher etorphine doses and use of hyaluronidase were associated with significantly shorter induction times, lower body temperatures, shorter distances moved, and reduced muscle damage as evidenced by lower CPK and lactate dehydrogenase levels (Kock, 1992). Although two accounts list 3 mg etorphine as a standard opioid immobilizing dose for wild black rhinoceroses (Kock, 1990; Rogers, 1993b), subsequent study suggests that 3 mg of etorphine is inadequate because of prolonged induction periods and associated capture stress (Kock, 1992). Based on review of published material and considerable author experience, 4 mg of etorphine is recommended as a

good standard dose for an adult black rhino bull or cow in good condition (Table 48.2) (Morkel, 1989, unpublished data). A scaled-down opioid dose should be used in young animals or those in poor body condition; however, in all other circumstances a low dose of etorphine is contraindicated for free-range capture of the black rhinoceros (Kock, 2006). Azaperone is incorporated into etorphine-based African rhino immobilization protocols at 100 to 250 mg total dose (Table 48.2) with a lower dose of 40–60 mg azaperone used for crating. Xylazine or Detomidine alone (100 or 10 mg per adult, respectively) can be substituted for azaperone based on individual preference.

There appears to be a slight disparity in the opioid dose required for immobilization of the various subspecies of black rhinoceroses. The desert subspecies (*Diceros bicornis bicornis*) needs a slightly higher dose than the other subspecies. Although 5 or even 6 mg etorphine may be necessary for an adult *D. b. bicornis* bull in good condition, 4 mg is usually more than adequate for a comparable response in animals of the *D. b. minor* or *D. b. michaeli* subspecies. Not only is there variation among subspecies, but there also appears to be some difference among individuals. Therefore, the capture veterinarian must be aware of these vagaries in dose response and be prepared to respond if an animal reacts unfavorably.

Asian Rhinoceros Wild Anesthetic Regimens Indian or Greater One-Horned Rhinoceros (Rhinoceros unicornis) Techniques for field anesthesia of the greater one-horned rhinoceros were developed to meet research needs, including the elucidation of basic ecology, genetics, social organization, and dispersal biology (Dinerstein, 1990, 2003). Furthermore, translocation programs are proving essential for reaching long-term population management goals for Rhinoceros unicornis in India and Nepal. Capture of wild greater one-horned rhinoceroses is usually conducted from atop trained elephants to facilitate finding and darting of rhinos among the dense tall-grass habitats in the flood plain grasslands and riverine forests where these rhinos live. In addition to providing an elevated platform, elephants (10–15 animals) are used to surround the target rhino before and after darting to facilitate observation of the rhino during induction and prevent escape into open water (Dinerstein, 1990).

Adult greater one-horned rhinoceroses weigh an estimated 2,000 kg, with males slightly larger than females. Dinerstein and colleagues immobilized 39 animals (representing 51 events) using a combination of etorphine and acepromazine (2–2.5 mg and 10 mg, respectively) delivered via remote IM injection either in the shoulder or rump using Cap-Chur darts with 5-cm needles (Table 48.2) (Dinerstein, 1990). One adult female was immobilized with carfentanil (0.7 mg) and all animals were successfully reversed in the field using diprenorphine

HCl (M50:50). Induction times were found to be significantly longer in breeding versus non-breeding males with the former group rarely moving far from the site of darting. A large disparity in induction times was noted across all age and sex groups presumably related to variable drug delivery from dart placement among the thick skin folds characteristic of the species (Dinerstein, 1990).

Javan or Lesser One-Horned Rhinoceros (*Rhinoceros sondaicus*) There have been no published reports describing field capture or anesthesia of the Javan rhinoceros. As with the Sumatran rhino, pitfall trap methodologies rather than stockade-style traps are recommended for capture of lesser one-horned rhinoceroses in the rainforest environment, provided the risks of flooding can be controlled (Nardelli, 1987b; Sadmoko, 1990). Field anesthesia is also possible—especially where animals are pushed out of the forest by human

activities—and would be based on extrapolation of the best available information from the other Asian species.

Sumatran Rhinoceros (*Dicerorhinus sumatrensis*) Several intensive operations have been conducted to capture wild Sumatran rhinos using corral or stockade traps with little or no success (Abdullah, 1987; Sadmoko, 1990). In one instance an adult female Sumatran rhino suffered severe head injuries and acute death following capture in a stockade trap from apparent panic-related self-trauma (Nardelli, 1987a). Planned capture of wild Sumatran rhinoceroses in the forests of Southeast Asia is most effectively accomplished by use of the pitfall trap. Effective pitfall traps measured $10' \times 4' \times 8'$ (length \times width \times depth) and incorporated strong plywood walls to preclude landslides and a breakaway false ceiling that drops the animal into the excavated pit beneath (Figure 48.7). Site selection favoring heavily used rhino trails

Rhinoceros Pitfall Trap

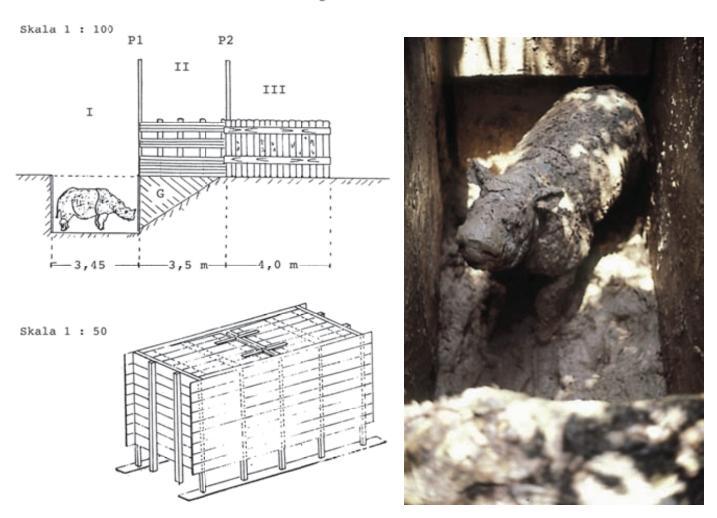


Figure 48.7. Diagrammatic sketch of pitfall capture method used in Indonesia's Riau Province for capture of wild Sumatran rhinoceros (Dicerorhinus sumatrensis). (Sketches adapted from Sadmoko AS. Study on capture techniques of Sumatran rhinoceros (Dicerorhinus sumatrensis, Fischer, 1814) in Riau Province. Bogor, Indonesia: Department of Forest Resource Conservation, Faculty of Forestry; Bogor Agricultural University (IPB), 1990. (Image courtesy Mohd Khan bin Momin Khan, Malaysia Department of Wildlife and National Parks.)

was considered the single most important criteria for success or failure of the pitfall trap (Abdullah, 1987). Nevertheless, pitfalls suffer from significant problems. In many Sumatran rhino areas poor drainage results in flooding of the pit despite careful preventive measures. Interference from non-target species is also a common hazard; tapir, elephants, cattle, and even human beings have fallen into pitfall traps despite sign boards erected for the benefit of man (Abdullah, 1987).

Because of the dense nature of the rainforest environment and rare sighting of individual rhinos therein, routine chemical capture techniques developed for Asian and African rhinoceroses are too dangerous as an animal may be lost in the darting process. Increasingly, however, animals are being pushed from the jungle by human encroachment and once beyond the protective boundary of the forest are immediately threatened. In these circumstances, pitfall capture methods are not feasible and chemical capture techniques are indicated. Therefore, the capture process for an at-risk Sumatran rhinoceros found wandering within a Southeast Asian village or otherwise outside a protected area should be approached with careful planning of some urgency. Once the appropriate National Park, Rhino Protection Unit (RPU) and Sanctuary staff have been contacted, the following stepwise approach to capture and translocation is suggested (Radcliffe, 2002).

Guidelines for Capture of Displaced Sumatran rhinoceros

Secure Immediate Area In the event a wild Sumatran rhinoceros is found wandering outside a protected area the first priority would be to secure the area from villagers and would-be poachers to prevent the animal from being shot or otherwise harmed before capture or relocation of the rhino is possible.

Determine Relocation Strategy If possible, a small core group of decision makers should be formed to make immediate assessment of the risks and benefits of rhino relocation. If the rhino were unharmed and close to a protected area (less than 10 km), then it would be desirable to move the rhino back into the forest. If the animal were injured or otherwise in need of medical attention or far (greater than 10 km) from the forest, a decision should be made to capture the animal.

Make a Plan for Rhino Capture Considering the high risks associated with capture by the "chase to exhaustion" method (i.e., rhino is captured following an extensive stressful chase without the use of routine chemical capture methods) (Figure 48.8), this approach should only be attempted as a last resort. The following are suggested guidelines and methodology for capture of at-risk Sumatran rhinos outside a protected area.

Capture Method One: Field Capture Using Chemical Restraint If a trained capture team is available (i.e.,

within 5 hours travel time) then it may be wise to have the RPU ranger staff carefully monitor and secure the rhino and surrounding area from a distance without pushing the animal to run as they await the capture team. A rapid induction and recumbency will be essential for safe capture of a tropical ungulate species such as the Sumatran rhino that may risk drowning or suffer from capture myopathy.

For field anesthesia of the Sumatran rhinoceros a combination of equal parts butorphanol and azaperone (80 mg each) is recommended for simplicity and its inherent safety for both rhino and people alike (Table 48.2) (Radcliffe, 2002). However, if a well-trained veterinary capture team is available, then use of more potent opioids such as etorphine combined with azaperone and hyaluronidase (2 mg, 80 mg, and 5,000 IU, respectively) or the newer etorphine-butorphanolmidazolam protocols may be considered depending on the situation. If the rhino is already compromised from a chase or is restrained by a snare, the use of the safer butorphanol protocol is preferable to the potent opioids (Table 48.2). The butorphanol-azaperone combination may require confinement within a temporary boma or some additional restraint via a body or head rope to facilitate crating in healthy animals.

Capture Method Two: Field Capture by Erecting Temporary Boma The Sumatran rhinoceros is perhaps the only species of rhino that can be captured by human physical restraint alone, albeit after much chasing and associated capture stress. Therefore, if a trained capture team is not available and the rhino is in immediate peril, physical capture can be a feasible option. To begin, follow the animal from a safe distance and without excessive chasing until the rhino is located within an area where it is resting and approachable (i.e., in water or other suitable location) (Figure 48.8). Large rolls of shade cloth or tarp are then carefully erected without disturbance to form a temporary boma surrounding the rhino that facilitates sedation, crating and transport. Once the animal is restricted within the confines of the "artificial boma," hand injection or pole syringe delivery of the butorphanol-azaperone combination would facilitate safe crating and transfer. The boma method is not likely to eliminate the long chase periods and accompanying stress, but it was effective in the recent capture and relocation of a young adult Sumatran rhinoceros in Indonesia (Figure 48.9).

RHINOCEROS CRATING AND TRANSPORT

Walking a Rhino

If a crate cannot be placed directly in front of the anesthetized animal, the rhino can be "walked" a distance and guided into the crate (Figure 48.10 and Table 48.3). When the rhino becomes recumbent, the blindfold, cotton wool, head rope, and brake rope are applied. Four to



Figure 48.8. Like the other rhinoceros species, the Sumatran rhinoceros (Dicerorhinus sumatrensis) is prone to capture myopathy. Here a wild "hairy" rhino is restrained with a girth rope in hopes of moving the animal into a temporary boma. Hyperthermia is best avoided by limiting chase periods and liberal application of water. (Image courtesy Sugiyo, Wildlife Conservation Society, Indonesia Program.)

six people are stationed on each rope, two people on each shoulder, one person to the side leading the team, and two people walking in front of the rhino, clearing obstacles in its path. The rhino is given small incremental doses of IV nalorphine depending on species; doses vary, but as little as 20 to 25 mg may be needed in total (Table 48.3) (Kock, 2006). After each dose, wait a few minutes and check the rhino's response to the prodder or by squirting water in the ear. If there is no response, give another dose of nalorphine. Once the rhino stands, it should begin to stagger forward and can then be readily guided with the head rope and by the people on the sides. If the rhino moves too fast, go slowly with the head rope and pull the brake rope to slow the moving rhino. Particularly with young and female individuals it is important to slow the rhino as it approaches the crate so it does not traumatize itself upon entrance.

When walking a black rhino into a crate, very encouraging results have also been achieved using diazepam just prior to arousal of the recumbent rhino (Table 48.3). First administer 10 to 15 mg IV diazepam and then wake the rhino with nalorphine at 10 to 20 mg per mg etorphine plus 1 to 2 mg diprenorphine IV. This crating



Figure 48.9. A wild Sumatran rhinoceros (Dicerorhinus sumatrensis) undergoing "hand translocation" without use of chemical restraint after displacement from a protected forest reserve in Indonesia. Although this animal survived significant capture-related morbidity, chemical capture techniques are preferred if trained staff are readily available. (Image courtesy Chandra Putra, Way Kambas National Park, Sumatra.)



Figure 48.10. "Walking" an etorphine-immobilized white rhinoceros (Ceratotherium simum) using ropes and trained personnel to guide and stabilize the narcotized animal.

protocol results in a rhino that is well tranquilized for about 8 hours but does not push or traumatize itself in the crate. In our experience, animals off-loaded into a boma were calm for up to 18 hours. Crating captive rhinos has historically involved low doses of etorphine (<1mg). As with anesthesia, however, mixed agonistantagonist are effective alternatives. Butorphanol and azaperone are mixed with hyaluronidase in a syringe and given by hand injection. The rhino is lured into the crate with food or by waving a white flag. If the rhino does not enter, staff can place a blindfold and head rope and pull the rhino into the crate (Table 48.3).

Table 48.3. Suggested opioid reversal protocols for walking, crate loading and transport of adult African rhinoceros.

26.1 1		ing and Translocation of African Rhinoceros
Method	Reversal Drug or Opioid	Technique for Crating or Translocation
Nalorphine walking and crating Method	White Rhino Walking: 1 mg diprenorphine (M50:50) plus 40 mg IV nalorphine. Give further incremental 10–20 mg nalorphine IV up to 75 mg (Kock 2006) Crating: 2–3 × etorphine dose of mg diprenorphine (M50:50) IV (add 1–2 naltrexone if pushing in crate) Black Rhino Walking: Start with 10 mg nalorphine IV. Give incremental 5 mg doses every 5–10 min up to 20–40 mg (Kock, 2006) Crating: 10–20 mg nalorphine per mg etorphine plus 1–2 mg M50:50 IV (Morkel) AVOID myopathy in crating process by ensuring rhino does not squat in crate; use prodder plus repeat 1–2 mg M50:50 doses	Blindfold rhino; cover eyes completely and position rhino's head close to or inside crate door: black rhino very important to have head in door; white rhino not critical; keep ears plugged until crated or leave in for transport Place head rope; use 20-m soft nylon behind posterior horn with knot on side of head passing rope end through hole in crate Place break rope on rear leg just below hock; use 8 meter nylon rope Position 6–8 people on head rope and 3–4 people on break rope Reverse; WAIT 50 seconds (M50:50) or 90–120 seconds (nalorphine); use prodder or water in ear to stimulate rhino Walk rhino into crate by pulling on head rope, slow rhino with break rope or go slowly with head rope; guide rhino by ground personnel; slide and secure pipes in crate (most crates have horizontal pipes, some only have the doors) If black rhino pushes in crate give 1 mg naloxone or 0.6–1.2 mg diprenorphine IV; if white rhino pushes give 1 to 2 mg naltrexone IV; use prodder on forehead (not on backside) as needed to stop pushing
Diazepam: nalorphine crating method	White and Black Rhino 10–15 mg Diazepam IV ten minutes before "waking" rhino with reversal protocol Use standard crating methodologies above for white and black rhinos after giving diazepam	Give diazepam to recumbent rhino and wait 10 minutes Use same crating procedure as above using diprenorphine alone (white rhino) or nalorphine combined with diprenorphine (black rhino) This protocol eliminates much of the pushing often observed in the crate following diprenorphine or nalorphine reversal procedures Diazepam provides good sedation for ~8 hours especially in white rhino
Butorphanol crating method	White Rhino: 50 mg Butorphanol IV (Radcliffe, 2000a, unpubl. data). Crating Nervous White Rhino: Male, 120 mg Butorphanol plus 160 mg Azaperone IM Female, 100 mg Butorphanol plus 160 mg Azaperone IM Combine with 2000 IU Hyaluronidase and hand inject (Radcliffe and Lopez, unpubl, data).	Butorphanol is a useful agent for crating and transport of crate- conditioned rhinos in zoological settings: combine with Azaperone as needed
	Black Rhino: 25–50 mg Butorphanol IV at time of crating for conditioned animals	Butorphanol provides excellent sedation without concerns of excessive head pressing in crate and occlusion of nostrils in corner. Upon first signs of sedation, keepers entice rhino into crate using food or by waving a white flag; if rhino does not enter crate, apply blindfold and head rope; "walk" rhino into crate by pulling on head rope through front of crate; use prodder on backside. No reversal required for butorphanol once rhino is in crate Use low doses etorphine to crate rhinos from boma; combine with azaperone in black rhino; wave white flag on pole to lure rhino into crate
Etorphine: azaperone boma crating	White and Black Rhino: Boma-Crating: 0.7-1.2 mg etorphine IM (Kock, 2006) OR 0.3 mg and 0.5 mg etorphine for black and white rhino, respectively without need to reverse Crate Sedation: 0.05-0.15 mg Etorphine IM plus 100-200 mg azaperone IM Transport: 25-150 mg Zuclopenthixol acetate IM or 5-10 mg diazepam IV	Etorphine is the ONLY AGENT to calm an excitable rhino inside a crate For crate sedation: Nalorphine sedation wears off ~5 hrs post-crating; thereafter give etorphine every 2 hours for duration of trip If rhino is not excitable, give Azaperone up to 200 mg azaperone per 6 hours NOTE: Etorphine is not effective within 3–4 hours of diprenorphine use and 12–24 hours following reversal with naltrexone Avoid perphenazine in white rhino (if going to boma) as it causes anorexia; low dose OK if going straight to field

From Morkel, unpublished data; Radcliffe, unpublished data; Kock MD, Meltzer D, Burroughs R, eds. *Chemical and Physical Restraint of Wild Animals: A Training and Field Manual for African Species*. Harare, Zimbabwe: Zimbabwe Veterinary Association Wildlife Group and International Wildlife Veterinary Services, 2006; Rogers PS. Chemical capture of the white rhinoceros (*Ceratotherium simum*), 1993a, OR Chemical capture of the black rhinoceros (*Diceros bicornis*), 1993b. In: McKenzie AA, ed. *The Capture and Care Manual*. Pretoria, South Africa: Wildlife Decision Support Service and South African Veterinary Foundation.

Tranquilization during Transport

All black rhinoceroses require tranquilization during transport (even most crate-conditioned animals) to preclude excessive struggles and associated trauma (Table 48.3). Other rhino species tolerate transport better than black rhinos, but still often benefit from some sedation. The veterinarian must always travel with the rhino and be prepared to give additional sedatives or even narcotics if needed. It is imperative that the veterinarian anticipates the animal's tranquilization needs as waiting until the rhino is alert and bouncing around, will risk unnecessary trauma. Additionally, a cool animal is generally more relaxed than an overheated one.

Rhinos settle into the rhythm of transport quite well after just a few hours. However, as the short-acting tranquilizers begin to wear off, the animal may become very excited if suddenly startled (i.e., from stopping, offloading, etc.). It helps to re-dose the rhino with tranquilizers while the vehicle is in motion or alternatively, stop, inject, and start moving again immediately. In most instances, hand injection is the best method to deliver additional tranquilizer. Insert a 20-gauge 1.5-in. needle into the lateral muscles of the neck while avoiding the nuchal region. Once the rhino has settled, attach the syringe and inject. A pole syringe can also be used, but beware of coring, as the rhino's skin may block the needle. Keep in mind that an IM injection takes 5 to 10 minutes for first effect. For a faster response, an IV injection into the ear vein is sometimes possible, although care must be taken to avoid the dangerous area around the animal's head and horn. Resting by the rhinoceros during transport can be beneficial or a potential problem, depending on the rhino's position and duration of recumbency. If the rhino lies down while the vehicle is moving, the rocking and bouncing action of the truck helps to facilitate limb circulation. Beware, however, if the rhino lies down for a long period (greater than 30 minutes) in a stationary vehicle unless you are very comfortable with its position. Rhinos heavily sedated with opioids often struggle to work out a way to lie down; however, if they manage to do it once, they will lie down more easily thereafter.

Short-acting tranquilizers such as azaperone, xylazine, and detomidine are useful agents to produce a calming effect in rhinos during transport. Azaperone is the tranquilizing agent of choice at 100 to 250 mg per adult and can be repeated every 6 hours as needed (Rogers, 1993a,b; Kock, 2006). A 40-mg per ml azaperone solution is a convenient preparation and mixes well with etorphine for IM administration to a fractious crated rhino. Examine azaperone solutions carefully before use, as they often crystallize under field conditions. The administration of opioids, either alone or in combination with IM azaperone or diazepam, is the only effective way to preclude an excited black rhino from traumatizing itself inside a crate (Table 48.3). Etorphine and azaperone (0.05-0.15 mg and 100-200 mg, respectively) are delivered by pole syringe with sedation achieved in 5 to

10 minutes for durations of 2 hours or more. Long-acting tranquilizers can help to calm an animal, however, are inadequate by themselves to sedate an excited animal during transport. Zuclopenthixol acetate (Clopixol Acuphase; 25–150 mg per adult rhino up to 400 mg) takes about an hour to provide sedative effects after administration, whereas perphenazine enanthate (Trilafon; 200–400 mg per adult) takes about 12 hours for first noticeable effects (Swan, 1993; Kock, 2006) (Table 48.3). Perphenazine works well for the translocation of black rhinoceroses, whereas caution should be exercised in white rhino, as its use has been implicated in anorexia (Portas, 2004; Kock, 2006).

ALTERNATIVE RHINOCEROS ANESTHESIA TECHNIQUES

Antidote Choice

Antidotes are best given IV in rhino, as response after IM injection is often slow and incomplete. Arousal of rhinoceros cow-calf combinations is the one instance in which IM injection of the antidote is preferred so the pair awakens slowly and has time to join together without dashing off in opposite directions. Following IV antidote administration, the rhino will stand up within 45 to 80 seconds. Rapid recoveries occur using the pure antagonists (naltrexone and naloxone) while longer recoveries are observed with the partial agonist-antagonists (diprenorphine and nalorphine). White rhino reversed with diprenorphine or nalorphine often require prodding. Response to the antidote is first noted at 40 seconds as an increase in the depth and rate of respiration and movement of the ears and eyes. Rhinoceroses get to their feet quickly and are immediately strong and aggressive. A rhino should always be moved into sternal recumbency before giving the antidote or it will bash its head on the ground as it attempts to rise from the lateral position. Re-narcotization has been reported in the white rhino, but it is a rare occurrence in the black rhino (Kock, 1990; Portas, 2004).

Out of tradition, opioid antagonists are dosed using empirically derived ratios rather than on a mg-per-kg basis; for the pure opioid antagonist, naltrexone, dosage ratios of 20 to 50 times the etorphine mg dose and 90 to 100 times the carfentanil mg dose are considered standard for captive rhinoceroses (Swan, 1993; Allen, 1996; Kock, 2006). Field workers frequently use lower naltrexone doses (12.5:1 naltrexone to etorphine ratio) without a problem (Kock, 1995); however, sedative signs at these doses have been reported in white rhino and a minimum of 40:1 is recommended to preclude re-narcotization (Rogers, 1993a; Kock, 1995; Portas, 2004). Although naltrexone is considered the agent of choice for complete reversal of narcotic anesthesia, a number of scenarios arise under both captive and field conditions in which a full reversal of an opioid-based procedure is undesirable.

The choice of antagonist and its desired action is dependent on two factors: species and location. Black

rhino are reversed into a crate with nalorphine alone or perhaps with 1 or 2 mg of diprenorphine (Kock, 2006; Morkel, unpublished data) (Tables 48.2 and 48.3). In the boma, Diceros bicornis are reversed with naltrexone, although very nervous or aggressive individuals may benefit from reversal with diprenorphine. Diceros bicor*nis* are completely reversed in the field using naltrexone; however, because it is expensive and difficult to obtain a combination of naltrexone and diprenorphine is often used for field reversal. In this case, give the standard diprenorphine dose (2–2.5 times the etorphine dose) (Swan 1993) by IM injection together with 10–20 mg naltrexone. In marked contrast to black rhino, white rhino are reversed into a crate using diprenorphine with perhaps 1 or 2 mg of naltrexone. In the boma and field, Ceratotherium simum are always reversed with naltrexone. Diprenorphine is often used for transport of Ceratotherium simum since its partial agonist-antagonist actions provide significant narcosis during travel. However, diprenorphine has minimal agonist effects in Diceros bicornis; therefore, they should be used judiciously for transport in this species. For any partial antagonism in a crate situation it is critical that the rhino be monitored very carefully to prevent excessive head pressing and occlusion of the airway or damage to the neck and limbs. A cattle prodder is a vital piece of equipment in managing sedated rhinos during travel.

Other Drugs and Immobilization Doses

Rhinoceroses can also be immobilized with the other potent opioids carfentanil, fentanyl, and thiafentanil. The following drug dosages are indicated for adult freeranging rhino in good condition:

- Carfentanil at 2.5–3.0 mg for adult African rhino Hofmeyr, 1975; De Vos, 1978). Carfentanil produces a quick induction and it is not necessary to combine with azaperone or xylazine.
- Etorphine at 1.8 mg plus 30 mg fentanyl (black rhino) (Rogers, 1993b; Kock, 2006).
- Fentanyl alone at 60 mg (black rhino) (Rogers, 1993b).
- Thiafentanil is mixed equally with etorphine. The adult rhino dose is 2 to 2.5 mg thiafentanil plus 2 to 2.5 mg etorphine. This mixture gives a faster induction time than etorphine alone. The usual antidotes for etorphine work well.

Rhinoceros Anesthesia Complications

With opioid-induced cardiopulmonary depression common in anesthetized rhinoceroses, the need may arise to deliver artificial ventilation. For emergency respiratory support in a rhinoceros, push the animal onto its side. A large person uses the knee of one leg (with foot placed firmly on the ground) to vigorously force the abdomen diagonally upward and forward against the diaphragm. This moves the diaphragm, forcing air into and out of the lungs and keeps the animal alive while

the IV opioid antagonist takes effect. When one leg is tired use the other leg and recruit additional people to assist. Jumping on the ribs or back of the rhino is ineffective and does nothing but fracture ribs and inflict unnecessary trauma.

Myopathies are common in rhinoceroses that experience excessive chase periods, impaired limb circulation with sternal recumbency or hyperthermia during capture (Figure 48.11). An especially critical period occurs at the time of crate loading and initial transport during field translocation of rhinoceroses. If stimulated to rise too early after partial reversal or with excessive tranquilization, animals may enter the crate and assume a rigid, semi-squatting position with their hind legs. This is undesirable and must be resolved quickly before the muscles are irreversibly damaged (Figure 48.11). Use of the electric prodder on the head never on the hindquarters can often stimulate the animal to rise and stand. If this does not work consider prompt IV administration of diprenorphine or nalorphine. A sling can also be placed under the belly of the animal, just in front of the rear legs to lift the hindquarters (using the crane on the recovery truck) until the strength has returned to the hind limbs.

A very small percentage of black rhinoceroses develop an adverse reaction that the author refers to as the "fat nose syndrome" (Morkel, unpublished data). Essentially the nostrils close up and appear edematous with a much-reduced opening to the nares. The anesthetist is often forced to hold open or pull the nostrils apart. It may indicate a hypersensitivity reaction; morphine is known to cause histamine release in humans and perhaps etorphine—derived from the same group of opium alkaloids—can produce the same uncommon effect in susceptible rhinoceroses.

New Field Anesthesia Techniques

Today's understanding of Rhinocerotidae anesthesia is truly the embodiment of many courageous pioneers



Figure 48.11. Post-translocation myopathy in a black rhinoceros; capture complications are more prevalent in animals that experience excessive chase periods, hyperthermia, or struggle to stand upon crating. (Image courtesy Birgit Kötting, Etosha Ecological Institute, Namibia.)

who led by exciting experimentation and hard-won experience (Harthoorn and Lock, 1960; Player, 1972; Young, 1973; Kock, 2006). Yet with the immense challenges inherent in practical anesthesia of these complex mammals, innovative procedures are welcome. The newest ideas for rhinoceros anesthesia are arising from a combination of practical experience and a desire to explore the depths of pharmacology. Nowhere are such explorations more exciting than the emerging science of mixed opioid receptor action on central nervous system activity (Chindalore, 2005). Various opioid receptor affinities and their pharmacological action are well described in humans but remain little understood in animals, including the rhinoceros, which is certain to be unique in many respects. Indeed the most exciting of these novel investigations is, perhaps, the incorporation of mixed agonist-antagonist opioid cocktails as part of routine field capture methodologies for the African rhinoceros (Bush, 2005).

Recent work by Bush and colleagues combines a mixture of concentrated butorphanol (40-90 mg; 30 mg/ml solution) with etorphine and midazolam (2-3.5 mg and 25-50 mg, respectively) (Table 48.2) (Bush, 2005). The addition of butorphanol to the anesthetic combination of etorphine and midazolam produces enhanced muscle relaxation and oxygenation with improved physiological parameters compared with the standard protocol for white rhinoceros albeit with substantially longer induction periods (~ 10min.). Butorphanol is a mixed opioid agonist-antagonist; its agonist κ receptor produces analgesia and marked sedation, whereas the weak μ receptor antagonism reduces respiratory depression and rigidity. The weak σ receptor agonist stimulates respiratory drive. Etorphine is a µ agonist, causing respiratory depression and muscle rigidity. These adverse µ agonist actions are reversed by butorphanol and significantly reduce the cardiopulmonary depression typical of the pure opioids alone (Bush, personal communication).

Besides the marked improvement in oxygen saturation there is a decrease in heart rate closer to normal making the heart a more effective pump. Blood gas values reveal a more normal pH and PCO₂, whereas blood pressures remain lower than with the standard pure opioid agonist protocols. Administering diprenorphine, a µ antagonist, IV 12 minutes into the anesthetic episode reverses etorphine but not butorphanol further counteracting adverse μ effects of etorphine while preserving butorphanol sedation effects. Therefore, if inadvertent opioid overdosage should occur, compromised physiological parameters can be rapidly corrected without losing control of the animal (Bush, personal communication). These discoveries may help to bring field rhinoceros capture into the realm of safety realized with captive animals in which butorphanol-based protocols are now standard replacements for more potent opioids (Radcliffe, 2000a; Portas, 2004).

RHINOCEROS CALF ANESTHESIA

Captive Calf Protocols

Anesthesia of captive white and black rhinoceros calves is safely accomplished with butorphanol alone or in combination with detomidine (Radcliffe, 2000c; Langan, 2001; Gandolf, 2006). Because of high sensitivity to opioid agents, rhinoceros calves respond very well to sedation and anesthesia with mixed agonistantagonists, precluding many of the adverse cardiopulmonary depressant effects observed with more potent pure agonists of this class. Furthermore, a rapid onset of action is attained by IV delivery or a slower induction by IM administration with both methods proving safe and effective for serial anesthesia (Gandolf, 2006) (Table 48.4). The combination of the α_2 -agonist, detomidine, along with the butorphanol was thought to enhance muscle relaxation and depth of anesthesia with IM use in white rhino calves. Complete reversal is achieved using naltrexone at 4 to 5 times the butorphanol mg dose and yohimbine HCl (Yobine) or atipamezole at 0.125 mg/kg for antagonism of the α_2 -agent.

Cow and Calf Field Capture

Field immobilization of juvenile rhinoceroses is not without inherent risk, as calves may separate from their dams after darting or become recumbent at different times despite concurrent drug delivery (Figure 48.12). Additionally, calves are more susceptible to capture stress, hyperthermia, and post-capture morbidity and mortality in boma situations (Kock, 1995). Translocation of cows with calves less than 18 months of age can be traumatic and is best avoided, whereas movement of very young calves 2 to 3 months old is particularly high risk. Even with successful translocation, it can be difficult to reunite the cow and calf, as the stress of capture and confinement often results in adult aggression directed toward the calf or the cow drying up. Methods for opioid sedation (0.2 and 0.05 mg etorphine for a cow and calf, respectively) have been used to facilitate boma reintroduction of cow-calf combinations (Kock, 2006). The wild black rhino cow is solitary by nature and usually retreats to a quiet spot to calve and stays there for the first month afterward. Therefore, if a black rhino gives birth in a boma, she rarely manages to raise the calf.

Opioid doses lower than those reported for adult animals are used for juvenile rhinoceroses with subadults receiving approximately one-half the adult dose. For example, when combined with a tranquilizer subadult African rhino (age approx 2.5 years) should receive 1.75 to 2 mg etorphine, whereas very young calves (age 2–3 months) can be immobilized with as little as 0.5 mg etorphine (Rogers, 1993a,b) (Table 48.4). A marked difference is observed in the escape behavior of African rhinoceros cow-calf pairs and should be anticipated during the chase and capture. White rhino calves run ahead of their mothers, whereas black rhino calves

run close at their mothers' heels (Kock, 2006). Additionally, the bond between white rhino cow-calf pairs is much stronger, making separation or splitting a more likely sequela in the black rhino.

When darting a cow with a calf from a helicopter, a fixed-wing aircraft is desirable to circle the capture site to assist with spotting. As a general rule, dart the cow first and about a minute later dart the calf (Kock, 2006). If the timing and darting are good, the pair will often go down together. Should the pair split up, the fixed-wing aircraft can stay with one animal. In open country

where visibility is good, the calf can be darted once the cow shows early signs of narcosis. In more thickly vegetated country where it is difficult to observe two separated animals, it is better to wait until the cow shows marked effects or is even recumbent before darting the calf. If the calf splits from its mother, the position of the immobilized mother can be taken by GPS or marked with a smoke grenade or toilet paper and the calf followed. Losing sight of a darted rhino must be avoided; therefore, it is mandatory to have experienced trackers as part of the ground team. When darting a cow-calf pair

Table 48.4. Suggested doses for immobilization and anesthesia of rhinoceros calves under both captive and wild conditions.

	Captive Calves				Wild Calves	
Rhino Species	Protocol	Reversal	Reference Comments	Protocol	Reversal	Reference Comments
White rhinoceros	10–20 mg Butorphanol (BT) IV for 66–159 kg calf (dose 0.13–0.15 mg/kg IV)	Naltrexone at 5 mg per mg BT	Gandolf, 2006 Heavy sedation Light anesthesia	Calf: 0.5–1 mg Etorphine (M99) Juvenile: 1.5–2.5 mg Etorphine Subadult: 3–3.5 mg Etorphine	Diprenorphine μ50:50 at 2.5 mg per mg Etorphine for transport	Kock, 2006 from SANP NOTE: Always dart mother rhino 30–60 seconds
			Mild resedation noted 8 hours post-reversal in one calf	NOTE: All white rhinos	Naltrexone at 40 mg per mg Etorphine including	BEFORE calf
				calves get 1 mg Diprenorphine μ50:50 plus 10 mg nalorphine ASAP upon recumbency to provide respiratory support		
	2.5–5 mg Butorphanol + 1.5–1.8 mg Detomidine (DET) IM for 69–122 kg calf (dose 0.03 mg/kg BT plus 0.07 mg/kg DET)	Naltrexone at 4 mg per mg BT Yohimbine at 0.125 mg/kg	Gandolf, 2006 Surgical anesthesia	Calf: 1 mg Etorphine + 15–20 mg azaperone Subadult: 2 mg Etorphine + 30–40 mg azaperone	Diprenorphine at 3 mg per mg Etorphine	Rogers, 1993a
Black rhinoceros	25 mg Butorphanol IV for ~500 kg subadult calf	Naltrexone at 5 mg per mg BT	Radcliffe, 2000c Heavy standing sedation	Calf: 1 mg Etorphine Subadult: 2 mg Etorphine	Naltrexone at 40 mg per mg M99	Kock, 2006 from SANP
		Ü		Calf: 0.5 mg Etorphine + 50 mg Azaperone Subadult: 1.75 mg Etorphine	Diprenorphine at 3 mg per mg Etorphine	Rogers, 1993b Kock, 2006
				+ 100 mg Azaperone NOTE: Do not use the D μ50:50 plus nalorphi black rhinos as it will arousal INSTEAD: 5 m Nalorphine IV; titrate	ne protocol in cause ng	NOTE: Always dart mother rhino 30–60 seconds BEFORE calf
Greater one- horned rhinoceros	Butorphanol IV or IM Use white rhino as model	Naltrexone at 5 mg per mg BT	Author suggestion based on use in African rhino calves	Calf: 0.5–1 mg Etorphine + 5 mg Acepromazine Subadult: 2–2.5 mg Etorphine + 10 mg acepromazine	Diprenorphine at 2.5 mg per mg Etorphine	Dinerstein, 1990 Same dose used for adult/ sub-adult

From Dinerstein E, Shrestha S, Mishra H. Capture, chemical immobilization, and radio–collar life for greater one-horned rhinoceros. *Wildl Soc Bull* 1990;18:36–41; Atkinson MW, Bruce H, Gandolf AR, et al. Repeated chemical immobilization of a captive greater one-horned rhinoceros (*Rhinoceros unicornis*), using combinations of etorphine, detomidine, and ketamine. *J Zoo Wildl Med* 2002;33:157–162; Gandolf AR, Wolf TM, Radcliffe RW. Serial chemical restraint for treatment of decubitus ulcers in two neonatal white rhinoceroses (Ceratotherium simum). *J Zoo Wildl Med* 2006;37:387–392; Kock MD, Meltzer D, Burroughs R, eds. *Chemical and Physical Restraint of Wild Animals: A Training and Field Manual for African Species*. Harare, Zimbabwe: Zimbabwe Veterinary Association Wildlife Group and International Wildlife Veterinary Services, 2006.



Figure 48.12. Anesthesia of rhinoceros calves is challenging, particularly under field conditions in which darting of the cow-calf pair must be well coordinated in order to limit stress on both parent and offspring.

on foot, the calf usually stays close to its immobilized mother. If approached carefully, the calf can be darted and generally becomes recumbent close to its mother. Note that black rhino calves are skittish and run off more easily than white rhino calves.

Wild subadult greater one-horned rhinoceroses have been immobilized using the same dosage as adult animals (2–2.5 mg etorphine plus 10 mg acepromazine) (Dinerstein, 1990). However, sub-adult animals proved more difficult to capture and often evaded dart attempts by outrunning the trained elephants that are commonly used for field immobilization of greater onehorned rhinos in the tall grassland habitats of India and Nepal. Indian rhinoceros calves were immobilized with 0.5 to 1 mg etorphine and 5 mg acepromazine using shorter 2.5 cm Cap-Chur needles. As with capture of African rhinoceros cow-calf pairs, it is recommended that greater one-horned cows be immobilized before their calves. Calves did not run away and were easier to capture if the mother was immobilized first to avoid trampling risk to calves or aggression toward the ground crew (Dinerstein, 1990).

Conclusion

During the Indian Mutiny a British soldier fired a bullet into the regiment's cherished mascot, a rhinoceros. In a spirit of scientific inquiry the soldier was testing the long held-belief—a conviction still strongly held by many since Dürer's famous rhinoceros—that its skin was held together with rivets like a knight's armor and impenetrable to any volley a person could throw its way. To the surprise of royalty and commoners alike, the rhino quickly expired.

The future of the world's rhinoceroses will remain tenuous, as human conflicts over shared resources escalate and rhino horn continues to be cherished by traditional Asian societies for supposed unicorn-like mythical properties. Nevertheless, it is comforting to know that humans, although solely responsible for the current crisis, are also simultaneously making strides to save the relic rhinocerotoids from their greatest enemy, ourselves. Safe anesthesia of wild and captive rhinoceroses alike will help scientists realize these conservation goals. Let us not make the same mistake as the British soldier and believe, naïvely, that the *armored* rhinoceros is invincible to the actions of our kind.

PRACTICAL STRATEGIES FOR RHINOCEROS FIELD ANESTHESIA

- Darts should be tested and prepared ahead of time, leaving only the drug-loading process to complete immediately prior to capture. Load the dart once you have visualized the rhino—tailoring the dose for size, age, and condition of the animal. The rhino should not be chased while the dart is being loaded. Dart quickly and back off.
- Dart sites must be given special care in rhinoceroses because of the propensity for abscess formation. Rhinoceros skin is thick and tough, making drainage of SC infections unlikely without appropriate wound care. Intramammary antibiotic preparations are common; however, the authors prefer infusion of 500 mg oxytetracycline directly into the dart wound. Oxytetracycline is a broad-spectrum antibiotic in high concentration, stable at room temperatures, viscous (it does not easily run back out of wound), and readily available.
- Tranquilizers are often combined with potent opioids to improve muscle relaxation in recumbent animals and help sedate and calm the rhino during transport.
- The addition of hyaluronidase, a hydrolytic enzyme that increases tissue permeability, greatly improves drug absorption and can markedly shorten the induction time. Xylazine or detomidine in mixture results in a slightly quicker induction and more salivation than azaperone.
- A lower opioid dose must be used for rhino that are in bomas, debilitated, old, or where you cannot get to the immobilized animal quickly (e.g., when darting on foot). Be very careful with animals in poor body condition. In most other situations underdosing of opioids is contraindicated for free-range capture of rhino.
- In general, any need for repeat darting of animals following partial or incomplete injection of immobilizing agents should redeliver the original full immobilizing dose. This is a useful rule for captive animals as well, since repeat darting is often associated with excitation and prolonged drug effects if titration is attempted.
- A rapid induction shortens the period the rhino is moving in a semi-narcotized state and thereby lessens the chance that the rhino will injure itself by encountering a hazard. This is especially true when immobilizing rhino in rough terrain. A quick induc-

tion also limits the exertion and physiological stress associated with increased body temperature, heart rate, oxygen consumption, and related physiological changes. However, caution must be used, as very rapid induction times are often associated with marked respiratory depression, especially in the more susceptible white rhinoceros.

- Nalorphine is useful in African rhinoceroses (Tables 47.2 and 47.3):
 - -To improve respiration, give 5 mg IV for black rhino and 20 to 30 mg for white rhino. Black rhino are very sensitive to nalorphine, so administer small incremental 5-mg doses given IV to effect. Nalbuphine (Nubain) may be used at approximately twice the nalorphine dose (20–40 mg) in a similar fashion for improving respiration in white rhino.
 - -To walk a rhino, start with 10 mg IV in black rhino up to a total dosage of 20 to 40 mg in 5-mg increments. For white rhino give 40 mg nalorphine IV followed by small incremental doses of 10 to 20 mg nalorphine up to 75 mg. Addition of 1 mg diprenorphine may help with arousal.
 - –For transport, wake the black rhino up into the crate with 10 to 20 mg IV nalorphine per 1 mg etorphine. You may also need to give diprenorphine IV at $2-3 \times$ etorphine dose if the animal is pushing or collapsing in the crate. Wake the white rhino with 1 mg diprenorphine plus 1 to 2 mg naltrexone if the animal is pushing in the crate.

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Non-domestic Suids

Luis R. Padilla and Jeff C.H. Ko

INTRODUCTION

The majority of the literature available on suid anesthesia and immobilization is derived from a single species: the domestic pig. Studies pertaining to anesthesia are limited in the documentation of physiological responses to anesthetic drugs, focusing instead on efficacy, induction and recovery times, and subjective descriptions of anesthetic quality. Therefore, the domestic pig is the physiological model for anesthesia of other species where appropriate, but readers seeking protocols for anesthesia of captive domestic pigs are referred to specific literature reviews on the subject (Moon and Smith, 1996; Smith et al., 1997; Swindle, 1998). We have included specific comments on Vietnamese potbellied pigs, since these are common exhibit animals in zoological institutions.

TAXONOMY

The suborder Suiformes includes the families Suidae and Tayassuidae, which encompass all pigs, hogs, babirussa, and peccaries. The generic term suid is commonly used to refer to members of both families. Table 49.1 is a list of known suid species, and adult weight ranges have been listed where available. The family Suidae includes pigs, hogs, and babirussa, and total 14 species in 5 genera. The Eurasian wild boar (Sus scrofa) is the wild ancestor of the domestic pig. Numerous breeds of the domestic pig (Sus scrofa) exist, an in many places, feral populations have been established in a free-ranging state, blurring the distinction between wild boar and domestic pig. The family Tayassuidae includes the peccaries or javelinas, currently found in three genera with one species each. A third family in the suborder Suiformes, Hippopotamidae, will be discussed in a separate chapter.

The main anatomical differences between the Tayassuidae and Suidae families are in dentition, tail length, hind limb anatomy, and the presence of a scent gland dorsally in the lumbosacral region in peccaries.

Sexual size dimorphism is more prominent in the Suidae than the Tayassuidae. The babirussa (*Babyrousa babyrussa*) has distinct features from the other members of the Suidae family, including a complex, sacculated stomach suggestive of foregut fermentation (Leus et al., 1999), and remarkable canines in the males.

GENERAL CONSIDERATIONS OF SUID BIOLOGY AND PHYSIOLOGY

All suids can be dangerous animals when approached. Most species have powerful jaws with sharp dentition, and individuals can be extremely fast and capable of inflicting severe wounds on humans. Canines grow as sharp tusks in many species, which is accentuated in males of the Suidae family. In addition, the short, strong limbs and muscular neck limit the possibility of physical restraint to juveniles or very small individuals. The use of snares and similar physical restraint devices used in domestic swine production is not recommended in non-domestic suid species owing to the high probability of injury to restrainer or animal. Many individuals fight aggressively when cornered or restrained, and sows can be very protective of their offspring. Suids can be capable climbers and agile jumpers that can escape from many situations or evade restraint.

Minimizing physiological stress prior to anesthetic induction is an important part of a successful outcome. Gregarious, social individuals are likely to be highly stressed if isolated for prolonged periods of time prior to anesthesia. If prolonged isolation is necessary, stress can be decreased by allowing visual contact between group mates. During anesthetic induction, it is preferable to isolate the target animal from the rest of a group to minimize the risk of trauma from companions.

Domestic pigs should be fasted for 24 hours (Moon and Smith, 1996), and non-domestic suids should be fasted for at least 12 to 18 hours (Calle and Morris, 1999). In addition to being at risk for vomiting and aspiration, inadequately fasted pigs are prone to gaseous distention

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The majority of the literature available on suid anesthesia and immobilization is derived from a single species: the domestic pig. Studies pertaining to anesthesia are limited in the documentation of physiological responses to anesthetic drugs, focusing instead on efficacy, induction and recovery times, and subjective descriptions of anesthetic quality. Therefore, the domestic pig is the physiological model for anesthesia of other species where appropriate, but readers seeking protocols for anesthesia of captive domestic pigs are referred to specific literature reviews on the subject (Moon and Smith, 1996; Smith et al., 1997; Swindle, 1998). We have included specific comments on Vietnamese potbellied pigs, since these are common exhibit animals in zoological institutions.

TAXONOMY

The suborder Suiformes includes the families Suidae and Tayassuidae, which encompass all pigs, hogs, babirussa, and peccaries. The generic term suid is commonly used to refer to members of both families. Table 49.1 is a list of known suid species, and adult weight ranges have been listed where available. The family Suidae includes pigs, hogs, and babirussa, and total 14 species in 5 genera. The Eurasian wild boar (Sus scrofa) is the wild ancestor of the domestic pig. Numerous breeds of the domestic pig (Sus scrofa) exist, an in many places, feral populations have been established in a free-ranging state, blurring the distinction between wild boar and domestic pig. The family Tayassuidae includes the peccaries or javelinas, currently found in three genera with one species each. A third family in the suborder Suiformes, Hippopotamidae, will be discussed in a separate chapter.

The main anatomical differences between the Tayassuidae and Suidae families are in dentition, tail length, hind limb anatomy, and the presence of a scent gland dorsally in the lumbosacral region in peccaries.

Sexual size dimorphism is more prominent in the Suidae than the Tayassuidae. The babirussa (*Babyrousa babyrussa*) has distinct features from the other members of the Suidae family, including a complex, sacculated stomach suggestive of foregut fermentation (Leus et al., 1999), and remarkable canines in the males.

GENERAL CONSIDERATIONS OF SUID BIOLOGY AND PHYSIOLOGY

All suids can be dangerous animals when approached. Most species have powerful jaws with sharp dentition, and individuals can be extremely fast and capable of inflicting severe wounds on humans. Canines grow as sharp tusks in many species, which is accentuated in males of the Suidae family. In addition, the short, strong limbs and muscular neck limit the possibility of physical restraint to juveniles or very small individuals. The use of snares and similar physical restraint devices used in domestic swine production is not recommended in non-domestic suid species owing to the high probability of injury to restrainer or animal. Many individuals fight aggressively when cornered or restrained, and sows can be very protective of their offspring. Suids can be capable climbers and agile jumpers that can escape from many situations or evade restraint.

Minimizing physiological stress prior to anesthetic induction is an important part of a successful outcome. Gregarious, social individuals are likely to be highly stressed if isolated for prolonged periods of time prior to anesthesia. If prolonged isolation is necessary, stress can be decreased by allowing visual contact between group mates. During anesthetic induction, it is preferable to isolate the target animal from the rest of a group to minimize the risk of trauma from companions.

Domestic pigs should be fasted for 24 hours (Moon and Smith, 1996), and non-domestic suids should be fasted for at least 12 to 18 hours (Calle and Morris, 1999). In addition to being at risk for vomiting and aspiration, inadequately fasted pigs are prone to gaseous distention

Table 49.1. Species of suids by family and weight ranges.

Species	Adult Weight	Common Name	Comments
Family Suidae			"True" Pigs
Sus scrofa	40-300 kg	Eurasian wild boar	Domesticated into farmed pigs, many wild "races" exist
·	32-100 kg	Vietnamese potbellied pig	Breed of domestic pig, commonly seen in zoos
Sus salvanius	6-10 kg	Pygmy hog	
Sus bucculentus		Vietnamese warty pig	
Sus verrucosus	35-185 kg	Javan warty pig	
Sus barbatus	100-200 kg	Bearded pig	
Sus philippensis		Philippine warty pig	
Sus cebifrons		Visayan warty pig	
Sus celebensis	40-70 kg	Sulawesi warty pig	
Potamochoerus porcus	45-120 kg	Red river hog	
Potamochoerus larvatus	50-115 kg	African bush pig	
Hylochoerus meinertzhageni	100-275 kg	Giant forest hog	
Phacochoerus africanus	50-150 kg	Common warthog	
Phacochoerus africanus	45-140 kg	Desert warthog	
Babyrousa babyrussa	40-100 kg	Babirusa	
Family Tayassuidae			Peccaries or Javelinas
Catagonus wagneri	30-45 kg	Chacoan peccary	
Pecari tajacu	15-35 kg	Collared peccary	
Tayassu pecari	25-40 kg	White-lipped peccary	

of the stomach, which may result in abdominal distention and compromise ventilation by altering pleural pressure and chest wall mechanics (Mutoh et al., 1991). Fasted suids often consume shavings, bedding material, or caging substrates if given access.

Suid skin is tough, tight, and not very pliable, and contains a significant subcutaneous (SC) adipose tissue layer. Injectable anesthetics administered into the adipose tissue layers result in variable or altered responses when compared with true intramuscular (IM) injections, which should not be mistaken for decreased drug efficacy or variable species susceptibility. The amount and distribution of fat varies with age, among species, breeds, or subspecies. Areas with thick fat deposits are less desirable for reliable injections. Injection into leaner muscle masses, such as the semi-membranosus, semi-tendinosus, or the dorsal prescapular muscle mass (Calle and Morris, 1999) is likely to result in more predictable effects. The choice of needle length is crucial to obtaining deep muscle injections, and a minimum length of 1.5 in. is suggested to assure IM placement in most adult animals.

Suids are prone to hyperthermia. All species have a relatively low surface area in a proportionately large volume body with a significant layer of SC body fat, and limited sweating capabilities for heat dissipation. Physical excitement or increased exertional activity prior to successful immobilization may result in muscular heat generation and elevations in core body temperature. Severe elevations in body temperature can be treated by cooling the skin surface with alcohol baths or placing ice packs around large vessels (Moon and Smith, 1996), using cool intravenous (IV) fluids, or, in extreme cases, using cold water enemas. Close temperature monitoring and good clinical judgment must be

used to prevent overtly aggressive rapid cooling and hypothermia.

Although hyperthermia can occur in any suid species, the syndrome known as malignant hyperthermia only occurs in domestic swine. Malignant hyperthermia syndrome of swine is a well-documented, autosomal recessive condition of domestic pigs resulting in abnormal skeletal muscle function because of defective calcium handling (Moon and Smith, 1996). Large white breeds of domestic swine are considered most susceptible, but it can occur in any breed or mixedbreed individual, including miniature potbellied pigs (Claxton-Gill et al., 1993). Manifestations of hyperthermia and muscle rigidity can be induced by stress, elevated ambient temperatures, inhalants and injectable anesthetics, paralytic agents, and other drugs. The body temperature of pigs can increase as high as 110°F (Moon and Smith, 1996), and muscle rigidity, tachycardia, tachypnea, hypoxemia, and cardiac arrhythmias can develop. Serum chemistries may show elevations in potassium, ionized calcium, myoglobin, and creatine kinase. Clinicians suspecting this condition should immediately institute supportive symptomatic therapy and discontinue inhalant anesthetics. Dantrolene, which has skeletal muscle-relaxing properties, is an effective treatment for this condition (Gronert, 1980), and can be used prophylactically in susceptible pigs. Other drugs that cause muscle relaxation might be used in managing hyperthermia.

VASCULAR ACCESS

The SC adipose tissue layer and the tight skin of most suids make vascular access a challenging task. Sedation

or anesthesia should be used to facilitate blood collection in non-domestic species, except in very small individuals. Blood can be collected from the jugular, femoral, cephalic, saphenous, tail (coccygeal), and auricular veins. Catheter placement is possible in the cephalic, saphenous, and auricular veins. Although other sites are described in this section, they are not recommended in most situations because of inherent technique risks.

Blood collection from the femoral vein is easy in most species, but caution must be taken to avoid lacerating the femoral artery. The femoral vein is easily reached by placing the animal on dorsal recumbency and slightly extending the leg caudally (Figure 49.1). The clinician palpates between the muscle bellies to find the femoral groove and a long needle (1 in. or longer, depending on the size and body condition of the animal) is advanced with slight negative pressure (Figure 49.2). After successful collection, pressure should be applied to minimize hematoma formation. Venipuncture on this site can be painful and suids may show some lameness after recovery, associated with deep hematoma formation or soft tissue trauma.

The cephalic and lateral saphenous veins can sometimes be palpated under the skin. In some species, such as warthogs and red-river hogs, these veins are easily palpated and accessible, but in others (*babirussa*) the veins roll under the skin. A clinician familiar with the orientation of these veins in most species might be able to blindly advance a small needle and obtain a blood sample. Blind catheterization of these veins is possible, although it is recommended that a scalpel blade be used to puncture the thick skin and avoid damaging the catheter stylette. A venous cut-down at the cephalic vein site should be attempted when catheterization is essential and not possible at other sites.

The coccygeal or tail vein is an adequate venipuncture site for collecting small volumes of blood in most species. In peccaries, the tail is relatively shorter and venipuncture is more challenging, but small volume samples (less than 3 ml) can still be collected if the needle is heparinized. The vein is located on the ventral midline. An individual can be placed on lateral recumbency and the vein is approached ventrally at the base of the tail, using a 21- to 23-gauge needle. If too much negative pressure is used, the vein can be easily collapsed.

Suids have thick, muscular necks, and the jugular is not palpable or visible externally. Some species, such as babirussa, may have redundant folds of skin around the neck that further limit access to the jugular vein. However, the jugular veins are large in all species. A long (greater than 1.5-in.) needle advanced cranially in the direction of the jugular furrow, with a slightly medial orientation while applying negative pressure, can be successful.

The auricular veins on the ears of domestic pigs are a common site for IV access, catheter placement, and blood collection. The veins are present on the dorsolateral



Figure 49.1. Immobilized babirussa positioned on dorsal recumbency for femoral vein blood collection. (Photo courtesy of Andrea Capobianco Dondona, Oklahoma City Zoo.)



Figure 49.2. Femoral vein blood collection in an anesthetized babirussa. Notice the leg is slightly extended caudally and the needle is placed on the femoral groove between muscle bellies. Pressure should be applied after blood collection to minimize hematoma formation. (Photo courtesy of Andrea Capobianco Dondona, Oklahoma City Zoo.)

aspect of the ear. Their usefulness in exotic suid species varies, but should be considered for quick vascular access or when injecting small volumes. Large-eared species, such as red river hogs and warthogs, may have prominent veins, but they are of negligible size in other species (babirussa and peccaries). Using topical alcohol to induce vasodilation and applying pressure at the base

of the ear may help identify the veins. A butterfly catheter can be secured around the flat (posterior) part of the ear, or a regular catheter can be glued in place with the inside of the ear rolled around gauze to provide rigidity and support in securing the catheter. One must keep in mind that most suid species have very sensitive ears, and even minor manipulations may result in complications after recovery (abnormal ear posture and rubbing ear on surfaces).

Orbital sinus puncture is used in some research laboratories for blood collection in domestic pigs, and a variation has been described and used successfully in collared peccaries (Lochmiller et al., 1984). A peccary is placed in dorsal recumbency, with the head extended and stabilized by holding the snout. A 16-gauge 1-in. long needle without a syringe is placed at the medial canthus of the eye, medial to the nictitating membrane. The needle is advanced approximately 2 cm at a slightly ventral, posterior angle through the conjunctiva, until the orbital sinus is reached. Blood will flow through the needle and can be freely collected in a tube placed under the hub. When collection is completed, the needle is removed and pressure is applied to the closed eyelid to stop blood flow. This technique is not likely to be popular with zoo staff or exotic pet owners, and potential complications exist. It is not recommended in most situations.

Anterior vena cava puncture is widely used for blood collection in domestic pig production, but is not without potentially detrimental effects, and can not be recommended for non-domestic suids. Risks of improper anterior vena cava puncture include vein laceration and cardiac tamponade (Moon and Smith, 1996). A technique has been described for chemically restrained collared peccaries, and the authors recommend it for obtaining large (greater than 20 ml) volumes of blood (Lochmiller et al., 1984). This technique was used in large numbers of anesthetized collared peccaries (*T. tajacu*) with no fatalities (Lochmiller et al., 1984). After placing a peccary in dorsal recumbency in a V-shaped trough, the head is extended slightly to stretch the sternocephalicus musculature. The site of needle entry is found by placing a thumb against the anterior portion of the manubrium of the sternum. The needle is inserted at a point equal to the width of the thumb anterior and lateral to the edge of the sternocephalicus muscle. The needle is directed caudally and angled dorsomedially at a 30- to 40-degree angle formed by the point of the sternum. In an adult peccary, the authors preferred a 21-gauge, 1.5-in. long needle.

ENDOTRACHEAL INTUBATION AND ANESTHETIC MONITORING AND SUPPORT

Sternal recumbency is recommended for endotracheal intubation, although lateral recumbency may be more practical for very large individuals, animals with large tusks, or obese and brachycephalic animals. Potbellied pigs may be easier positioned in lateral or dorsal recumbency. In these cases, suspending the head

slightly at the end of an elevated table or platform may facilitate positional manipulation. A common hurdle to successful endotracheal intubation is the difficulty in opening the mouth sufficiently to visualize and advance an endotracheal tube. This might be facilitated with a deeper plane of anesthesia or different drug combinations, but one must consider that the mouth does not open widely in some species, even in extremely relaxed individuals. In addition, the larynx of most suids is difficult to reach owing to the elongated shape of the head and distal location in most species.

Using soft gauze strips behind the upper and lower canines, an assistant can open the mouth and simultaneously position and extend the head slightly. Anatomical idiosyncrasies in suids make endotracheal intubation challenging, but familiarization with the anatomy and visualization of the tortuous route to the airway facilitates success (Figure 49.3). A long laryngoscope blade can be used to push the epiglottis and expose the larynx. A stylet can be passed into the larynx and then the endotracheal tube can be threaded over the stylet (Figure 49.4). Care must be taken with the



Figure 49.3. Endotracheal intubation in a pot-bellied pig. (Photo courtesy of Jeff C.H. Ko.)



Figure 49.4. Cross section of pot-bellied pig's head, showing the use of a laryngoscope and stylet to intubate the trachea. (Photo courtesy of Jeff C.H. Ko.)

advancement of the stylet. A stylet can damage the laryngeal mucosa and resulting laryngeal edema and airway obstruction. Also, if a stylet is passed too deeply the peribronchial tissues can be damaged, causing a pneumothorax (Thurmon, 1996). If the larynx is physically stimulated, laryngospasms, apnea, and subsequent cardiovascular collapse may occur as part of the laryngochemical reflex (Ko et al., 1993a). The reflex occurs commonly in domestic pigs, but the response can be ameliorated with a topical anesthetic, such as lidocaine on the larynx prior to attempts at intubation.

The endotracheal tube can be advanced into the larynx with the normal curvature of the tip pointing ventrally. The tube will encounter resistance as it reaches the posterior floor of the larynx, and rotating the tube slightly at this point facilitate advancement. Suids are obligate nasal breathers, and caution should be used when securing the endotracheal tube. Tying a tube too tightly around the nose or muzzle may cause significant congestion of upper respiratory passages, leading to difficult breathing during recovery. This consideration should be emphasized in brachycephalic individuals, such as potbellied pigs.

The same monitoring equipment used in other mammalian species can be used in anesthetized suids. However, the clinician should not rely on monitoring equipment alone, and visual or palpable assessment of respirations, pulse or heart rate, and mucous membrane coloration and capillary reflex times should not be ignored. Ocular positioning is not an adequate indicator of anesthetic depth in suids owing to the shallowness of the orbital socket.

A pulse oximetry probe can be placed on the tongue, ear, or vulvar or preputial folds. A rectal probe can be used, but mucosal contact must be confirmed by removal of feces. Most commercially available pulse oximetry units give a measure of pulse rate as well as saturation for oxygen, which provide a minimal but reliable data base of anesthetic monitoring. Interpretation of pulse oximetry values is more accurately done if respiration and ventilations are concurrently monitored.

Placing direct and invasive blood pressure monitors in anesthetized suids is impractical and time consuming, mostly owing to difficulties in arterial catheterization. Indirect blood pressure monitoring is recommended. Although no specific studies have been done in any exotic suid species, a close correlation between oscillometric methods of blood pressure monitoring and direct arterial blood pressure methods have been shown in domestic pigs (Moon and Smith, 1996). Trends seen in indirect blood pressure readings are more useful than absolute numbers recorded (Moon and Smith, 1996). If a commercially available indirect blood pressure monitor is not available, a simple method is to use a Doppler flow probe on the second digit to locate a pulse and place a cuff with a sphygmomanometer proximally over the metatarsus. A study done on domestic sows showed that similar cuff placement with a pulse

oximetry probe positioned distally on the second digit (instead of a Doppler flow probe), correlated closely with direct arterial blood pressure (Caulkett et al., 1994). Cuffs placed on the legs should be of a width between 40% and 60% of the limb circumference (Moon and Smith, 1996). Cuff placement on the legs can be above or below the carpus or tarsus, but the cuff bladder should be over the medial aspect of the leg. If the cuff is placed on the tail, the bladder should face ventrally (Moon and Smith, 1996). In prolonged procedures, or where direct anesthetic monitoring is essential, the femoral artery can be cannulated in most suids with some effort, although cut-down procedures may be necessary to facilitate access.

Capnography is a useful indicator of physiological state of anesthetized suids. In domestic pigs, elevations in end-tidal CO₂ are seen early in the onset of malignant hyperthermia before other signs appear (Moon and Smith, 1996). If not endotracheally intubated, trends can be monitored nasally if a proper fit is achieved. Most suids tend to hypoventilate under anesthesia, which may be a reflection of the most popular anesthetic protocols, large (maybe unfasted) stomach, obesity in most captive animals, or a combination of these. End-tidal CO₂ readings higher than 45 mmHg warrant ventilatory support, and possibly oxygen supplementation. Positive pressure mechanical ventilation should not exceed what is necessary for minimal visible chest expansion, and caution should be used to avoid exceeding 20 cm H₂O, which has been seen to cause spontaneous pneumothorax in healthy potbellied pigs (Lukasik and Moon, 1996).

The intranasal route is an easy and practical way to administer supplemental oxygen or anesthetic gas to suids, but should not be used for positive ventilation. Attempts at ventilating domestic pigs through nasal intubation have resulted in significant gastric distention, anterior displacement of the diaphragm, and decreased functional lung capacity (Thurmon et al., 1996). Improper intubation (i.e., esophageal instead of endotracheal) may result in similar complications.

Traditional electrocardiography "alligator" clips may be difficult to attach to the tight suid skin. Instead, 25-gauge needle electrodes can be inserted SC, or patch electrodes can be adhered to the skin after degreasing with acetone as has been described for domestic swine (Moon and Smith, 1996). Temperature can be measured easily rectally, or with a digital esophageal probe placed in either the esophagus or rectum.

ANESTHETIC COMBINATIONS

General Principles

The majority of immobilization scenarios for non-domestic suids will be to facilitate routine, minimally invasive procedures (e.g., relocation, physical examination, hoof trimming, blood collection), where a light plane of anesthesia or deep sedation will suffice. Deeper

planes of anesthesia can be achieved with inhalant anesthetics or supplemental doses of injectable anesthetics.

Numerous protocols are available for usage in non-domestic suid anesthesia and are summarized in Table 49.2. Most balanced combination protocols have fewer side effects than any single-drug protocol, since the different drugs may potentiate anesthetic effects and decrease the effective necessary dose of any single drug. In choosing a balanced anesthetic combination, it has been suggested that suids may be relatively more

resistant to opioids and α_2 -adrenergic agonists than other species, but relatively more sensitive to the effects of benzodiazepines (Moon and Smith, 1996).

Premedications

Pre-anesthetic sedatives can be used to decrease anesthetic drug doses, facilitate administration of the induction agent, or ease pre-anesthetic anxiety. Anecdotal reports of oral diazepam in warthogs (0.1–0.5 mg/kg) prior to anesthetic induction result in significantly

Table 49.2. Common immobilization protocols used in non-domestic suids.

Drug Combination	Dose (mg/kg)	Species Documented	Comments	References
Ketamine (K)	20 (K)	Collared peccaries	Not recommended as first choice for immobilization. Recoveries can be prolonged and violent. Fatality associated with ambient temperature	Hellgren et al., 1985; Gallagher, 1985
Ketamine (K)/ tiletamine-zolazepam (TZ)/medetomidine (M)	3.9 (K)/0.63 (TZ)/ 0.03 (M)	Chacoan peccaries	Prolonged recoveries despite medetomidine reversal with atipamezole, residual ataxia	Sutherland–Smith et al., 2004
Tiletamine-zolazepam (TZ)	2-5 (TZ)	Multiple species	Smooth induction, poor muscle relaxation, prolonged recoveries might be rough. Duration of recovery is dose dependent	Calle and Morris, 1999; Allen, 1992
	2.18 (TZ)	Chacoan peccaries	Prolonged recoveries, poor relaxation	Allen, 1992
Tiletamine-zolazepam (TZ)/ xylazine (X)	2.35 (TZ)/2.35 (X)	Collared peccaries	Prolonged recoveries, but study did not antagonize xylazine; Fatality associated with a double dose	Gabor et al., 1997
	1.23 (TZ)/1.23 (X)	White-lipped peccaries	Dose of 1.51 TZ and 1.51 X not successful in Collared peccaries	Selmi et al., 2003
	1.2-2.1 (X)/ 1.8-3.3 (TZ)	Babirussa	(X) administered as a premedicant, followed by TZ 20 min later. Antagonism with 0.14 mg/kg yohimbine and 1mg flumazenil for every 20 mg zolazepam. Bradycardia seen in some cases.	James et al., 1999
	3 (TZ)/0.5 (X)	Warthogs	Recoveries > 90 minutes	Sonntag et al., 2004
Tiletamine-zolazepam (TZ)/romifidine (R)	3.3 (TZ)/1.6 (X) 3-6 (TZ)/0.1 (R)	Feral pigs Wild pigs		Sweitzer et al., 1997 Siemon et al., 1992
Tiletamine-zolazepam (TZ)/ butorphanol (B)	1.46 (TZ)/0.14 (B)	White-lipped peccaries	Similar doses ineffective for collared peccaries	Selmi et al., 2003
-	1.26 (TZ)/0.36 (B)	Babirussa	Reverse with naltrexone, poor overall relaxation	Padilla, 2004
Medetomidine (M)/ butorphanol (B)/ midazolam (Mz)	0.04-0.07 (M)/ 0.15-0.3 (B)/ 0.08-0.3 (Mz)	Multiple Species	Bradycardia, Hypoxemia reported. Antagonize with atipamezole, naloxone or naltrexone, and flumazenil. Lower dose range used in calm, captive individuals.	Morris and Shima, 2003 (upper range)
Detomidine (D)/	0.06-0.125 (D)		,	Morris et al., 1999
butorphanol (B)/ midazolam (Mz)	0.3-0.4 (B)/ 0.3-0.4 (Mz)			
Xylazine (X)/	2-3 (X)/0.3-0.4 (B)/			Morris et al., 1999
butorphanol (B)/ midazolam (Mz)	0.3-0.4 (Mz)			
Detomidine (D)/ butorphanol (B)/ tiletamine-zolazepam (TZ)	2-3 (X)/0.3-0.4 (B) / 0.6 (TZ)			Morris et al., 1999

calmer individuals prior to immobilization, facilitating darting and minimizing complications (e.g., hyperthermia) associated with pre-anesthetic excitement. The use of xylazine prior to anesthetic induction with tiletamine-zolazepam has been reported in babirussa (James et al., 1999). However, the use of pre-anesthetic drugs is impractical in animals that can not be confined or where the anxiety of multiple injections clearly outweighs the practicality of a single darting event.

The use of anticholinergics as adjunct premedications with a sedative before anesthesia is advocated in domestic pigs (Moon and Smith, 1996), and should be considered in Vietnamese potbellied pigs. Anticholinergics decrease the likelihood of bradycardia, avoid bronchoconstriction, minimize airway secretions, and decrease salivation. Atropine (0.04 mg/kg) or glycopyrrolate (0.005 to 0.02 mg/kg) can be administered IM as part of pre-medicants. Glycopyrrolate is a more potent anti-sialogogue than atropine, but is also longer acting. Caution should be used when administering anticholinergics in conjunction with drugs that can cause peripheral hypertension, such as α_2 -adrenergic agonists.

Anesthetic and Sedation Protocols

Butyrophenones and Phenothiazines Azaperone is a short-acting butyrophenone neuroleptic designed for IM injection with a wide safety margin in domestic swine. Although its main use has been to decrease aggression in domestic swine, azaperone can be used alone as a reliable sedative, or as an anesthetic adjunct with dose-dependent effects. Doses of 0.25 to 0.5 mg/kg produce mild sedation without ataxia in domestic pigs (Braun 1993). Doses of 0.5 to 2.0 mg/kg reduce intraspecies aggression and cause mild ataxia, whereas doses of 2 to 4 mg/kg result in significant sedation and possible recumbency in adult pigs (Braun, 1993). However, doses exceeding 2 mg/kg are also more likely to cause negative drug effects, which are similar to those caused by phenothiazines, including hypotension, bradycardia, and decreased cardiac output and contractility. Priaprism has been reported in adult boars (Moon and Smith, 1996).

Although azaperone has not been used extensively in exotic suid immobilization protocols, it has a lot of potential as an anesthetic adjunct in non-domestic species, and has been used reliably in Vietnamese potbellied pigs. The recommended dose for potbellied pig sedation is 0.25 to 2.0 mg/kg, and doses of 2.0 to 8.0 mg/kg are suggested for anesthesia (Calle and Morris, 1999). Caution should be used at the higher range of the suggested dose.

Acepromazine is a phenothiazine compound used as a sedative adjunct in domestic pigs, but considered an inadequate sedative when used by itself (Moon and Smith, 1996). Its negative side effects are dose dependent and can be severe, including hypotension, decreased

heart rate, hypothermia, and decreased respiratory rate. However, acepromazine can be used to manage hyperthermia (Moon and Smith, 1996) and hypertension, or as a mild sedative adjunct.

Ketamine and Ketamine Combinations Ketamine has been used extensively in suid immobilizations. Despite a wide safety margin with minimal cardiorespiratory depressant effects (Tranquilli et al., 1983), suids exhibit muscle rigidity, and intubation is not possible. The use of ketamine alone requires high doses (15-25 mg/kg) to produce immobilization, and the quality of anesthesia is poor. Side effects include increased systemic and pulmonary arterial blood pressure, elevated heart rate, and increases in cardiac output and myocardial oxygen consumption. These effects can be ameliorated by administration of adjunct anesthetics or sedatives. Recoveries are rough, including hypersensitivity to stimulus and increased activity of the limbs (paddling), which may lead to hyperthermia, predisposing suids to self-trauma, pulmonary edema, and even death. Ketamine is not an ideal choice as a sole anesthetic agent due to the poor quality of anesthesia and rough recoveries, although it is a useful and relatively safe adjunct to balanced protocols.

Domestic pigs absorb ketamine rapidly, and almost completely, after intramuscular injection (Loscher et al., 1990). Anesthetic recovery in pigs occurs as ketamine is redistributed from the brain to other tissues, with drug excretion and metabolism being less critical for anesthetic duration. This is a significant consideration when choosing drugs for individuals with compromised organ function, since prolonged excretion is unlikely to affect duration of anesthesia. The elimination half-life of ketamine in healthy pigs is approximately 2 hours after IM or intravascular administration.

Ketamine has been used safely as a sole anesthetic agent in numerous peccary immobilizations (Hellgren et al., 1985). In collared peccaries (*Tayassu tajacu*), ketamine was used without detrimental, permanent effects at 20 mg/kg (Hellgren et al., 1985) administered IM. Prolonged recoveries (greater than 120 minutes) were seen when peccaries were immobilized with 15 to 25 mg/kg ketamine administered IM, and heat stress was seen in relation to ambient weather (Gallagher et al., 1985).

Some of the negative effects of ketamine anesthesia can be ameliorated with anesthetic adjuncts, which also decrease the ketamine dose required to achieve effective immobilization. α_2 -Adrenergic agonists, such as xylazine and medetomidine, are popular adjuncts to ketamine as a suid anesthetic. These combinations offer the advantage of being reversible to result in faster recoveries, but the reversal of the α_2 -adrenergic agonists is independent of the patient's ability to metabolize and clear ketamine. If the α_2 -adrenergic agonist is reversed

before ketamine is fully metabolized, recoveries can be undesirable, characterized by hyperkinesia of all limbs while recumbent, severe, and prolonged ataxia and distress vocalizations. It has been shown cardiac output decreased significantly for 30 minutes after administration of a ketamine (10 mg/kg) and xylazine (1 mg/kg) combination in domestic pigs, and arterial PO_2 decreased for 10 minutes, whereas total vascular resistance was significantly increased (Trim and Gilroy, 1985). It is likely that other α_2 -adrenergic agonists in combination with ketamine have similar effects in exotic suids, and should be used with caution.

Ketamine used in conjunction with benzodiazepines (diazepam, climazolam, or midazolam) offers better relaxation and smoother recoveries than ketamine alone. Midazolam is a more reliable IM sedative than diazepam because it is water soluble. Recoveries after ketamine-benzodiazepine combinations are prolonged, usually taking several hours. The administration of flumazenil may result in faster recoveries. However, if flumazenil is administered before ketamine has been totally metabolized, the recoveries are similar to those of ketamine alone.

A combination of 3.9 mg/kg ketamine, 0.63 mg/kg tiletamine-zolazepam and 0.03 mg/kg medetomidine was used to immobilize captive Chacoan peccaries (*Catagonus wagneri*) (Sutherland-Smith et al., 2004). Sufficient immobilization for handling was achieved at 12.6 ± 3.7 minutes, and good muscle relaxation was produced, although animals that were approached too soon after recumbency would be aroused and stumble away. Heart and respiratory rates declined, but oxygen saturation increased during anesthesia. Atipamezole was used to antagonize the medetomidine, but recoveries were still very prolonged (55–455 minutes) and showed residual ataxia.

Tiletamine-Zolazepam Combination A 1:1 ratio tiletamine-zolazepam combination has been used extensively in exotic suids (Calle and Morris, 1999), and can be used safely in any species. The combination offers the advantages of relatively low cost, wide availability and a wide margin of safety despite undesirable, but manageable, side effects. Commercially available formulations can be reconstituted to different concentrations, allowing for smaller volumes of induction. Induction times are rarely affected by increasing dose, but recovery times can be prolonged at higher doses. The dissociative anesthetic portion of this combination, tiletamine, is considered more potent than ketamine. Zolazepam, the benzodiazepine part of the combination, is likely responsible for prolonged recoveries. The use of flumazenil (1 mg flumazenil for 20 mg zolazepam IV or IM) (Calle and Morris, 1999) as a benzodiazepine antagonist may shorten recovery times, but the effects may be of short duration and animals may become more sedate as flumazenil is metabolized.

Anesthesia is characterized by relatively fast inductions, moderate relaxation inadequate for intubation, and prolonged, sometimes violent, recoveries. Most suids retain some degree of hyperresponsive reflexes, such as exaggerated limb withdrawal when stimulated. Heart rate and arterial blood pressure may increase. Respiration rate may decrease initially but minute ventilation is well maintained. Recoveries are characterized by repetitive motion of the legs (paddling) prior to standing, excessive salivation, altered thermoregulation, increased vocalizations and prolonged ataxia (Moon and Smith, 1996). Deaths have been reported occasionally in association with very rough recoveries (Morris and Shima, 2003).

Chacoan peccaries (*Catagonus wagneri*) were immobilized reliably and safely with tiletamine-zolazepam at a mean dose of 2.18 mg/kg IM (Allen, 1992). Anesthesia was induced in 7.6 minutes, but recoveries were prolonged (90–240 minutes) and some animals retained a dull mentation for up to 8 hours after immobilization. A more recent study (Sutherland-Smith et al., 2004) mentions that Chacoan peccaries anesthetized with 3.2 mg/kg tiletamine-zolazepam took longer than 8 hours to recover, which may be a function of higher doses, resulting in prolonged recoveries, as had been previously suggested (Allen, 1992).

Tiletamine-Zolazepam/\alpha_2-Adrenergic Agonist Combinations The addition of α_2 -adrenergic agonists adjuncts to tiletamine-zolazepam anesthetic protocols allows the usage of lower doses of tiletamine-zolazepam to achieve desired effects while improving overall muscular relaxation. The negative cardiovascular side effects involved with this addition are offset by the benefits of faster, smooth recoveries and better relaxation, often allowing for endotracheal intubation.

Xylazine has been a popular, inexpensive, and widely used adjunct to tiletamine-zolazepam immobilization protocols in non-domestic suid immobilizations. Commercially available formulations of tiletamine-zolazepam can be reconstituted with xylazine (Gabor et al., 1997), and immobilization protocols can be pre-determined by volume per weight to simplify dose calculations in the field. Since suids are considered resistant to the effects of α_2 -adrenergic agonists, most published reports recommend a relatively high dose of xylazine. In domestic pigs, it has been shown that the addition of xylazine to tiletaminezolazepam-based immobilization protocols increases relaxation to facilitate intubation (Ko et al., 1993b). Increasing xylazine dose in xylazine-tiletaminezolazepam anesthesia of domestic pigs enhances the quality of anesthesia, sedation and muscle relaxation without prolonging recovery (Ko et al., 1995).

Wild feral pigs (*Sus scrofa*) in North America were reliably immobilized with a xylazine (1.6 mg/kg) and tiletamine-zolazepam (3.3 mg/kg) IM combination

delivered to trapped pigs by blow dart (Sweitzer et al., 1997). Animals recovered and were released within 120 minutes of initial injection. Authors reported slight decreases in heart rates and body temperatures, but adequate respiration rates and blood oxygen saturation levels. Immobilization of a large number (n = 107) of collared peccaries (Tayassu tajacu) has been described using a tiletamine/zolazepam (2.35 mg/kg) and xylazine (2.35 mg /kg) combination, although the authors reported it as a combined average dose of 4.7 ± 0.9 mg/ kg (Gabor et al., 1997). One fatality was reported in a peccary receiving an overdose (9.78 mg/kg combined dose). Recovery times in peccaries were prolonged, being described as conscious at 64 ± 29 minutes and first standing at 92 ± 33 minutes from injection, but xylazine was not antagonized in the study. Selmi et al. (2004) used intramuscular tiletamine-zolazepam $(1.23 \pm 0.26 \text{ mg/kg})$ in combination with xylazine $(1.23 \pm 0.26 \text{ mg/kg})$ successfully in white-lipped peccaries, but similar doses $(1.51 \pm 0.29 \text{ mg/kg tiletamine})$ zolazepam and 1.51 ± 0.29 mg/kg of xylazine) were unsuccessful at providing immobilization in collared peccaries, undermining that species-specific differences must be taken into account.

In babirussa, xylazine (1.2–2.1 mg/kg IM) premedication followed by tiletamine and zolazepam (1.8–3.3 mg/kg) produced good relaxation, smooth inductions, and sufficient immobilization for minimally invasive procedures, although additional drugs were necessary to deepen or prolong anesthesia (James et al., 1999). The authors report bradycardia in some animals (range of 35–111 beats per minute) while maintaining good oxygen saturation and stable respiratory rates (James et al., 1999). Female babirussa required slightly higher induction doses to reach similar effects. A small study (Sonntag et al., 2004) showed that warthogs can be immobilized safely with tiletamine-zolazepam (3.0 mg/kg) and xylazine (0.5 mg/kg), although recoveries were prolonged (greater than 90 minutes).

Romifidine has not been used extensively in suids, but one report describes its use (0.1 mg/kg) as an anesthetic adjunct to tiletamine-zolazepam (3–6 mg/kg) in wild boars (Siemon et al., 1992). Because these doses of tiletamine-zolazepam alone may be sufficient to sedate swine, the benefits of romifidine are likely to be supplemental and improve overall relaxation.

Tiletamine-Zolazepam/Butorphanol Tiletamine-zolazepam (1.46 mg/kg) has been used successfully in conjunction with butorphanol (0.14 mg/kg) to immobilize white-lipped peccaries (*Tayassu pecari*), but similar doses are ineffective to immobilize collared peccaries (Selmi et al., 2003). However, similar doses of tiletamine-zolazepam (1.26 mg/kg IM) combined with higher doses of butorphanol (0.36 mg/kg) resulted in adequate immobilization of babirussa for elective procedures (Padilla, 2004), and similar doses can be used in pecca-

ries and warthogs, although relaxation is inadequate for intubation.

Medetomidine-Based Anesthesia Medetomidine has been shown to induce deeper planes of sedation than xylazine in domestic pigs (Sakaguchi et al., 1992a), making it a useful anesthetic agent for suid immobilization. At higher doses of medetomidine (greater than 0.08 mg/kg) depth of sedation does not seem to increase significantly in domestic pigs, but the duration of sedation does. The study also showed better analgesia with medetomidine when compared with xylazine. The anesthetic properties of medetomidine can be potentiated by butorphanol when administered to pigs at 0.2 mg/kg (Sakaguchi et al., 1992b), and the combination is safe when administered to atropinized pigs (Sakaguchi et al., 1993). Medetomidine effects in domestic pigs can be antagonized with atipamezole at 2 to 4 times the medetomidine dose (Nishimura et al., 1992), although most clinicians prefer to use a 5:1 atipamezole:medetomidine ratio for antagonism (Morris and Shima, 2003).

Similarly, medetomidine effects can be potentiated when used in combination with midazolam (Nishimura et al., 1993). The cardiopulmonary effects of a medetomidine (0.04 mg/kg) and midazolam (0.2 mg/kg) combination in swine include a rapid increase in arterial and pulmonary arterial pressure owing to peripheral vasoconstriction (Nishimura et al., 1994). The antagonism of medetomidine with atipamezole resulted in a decrease in peripheral vascular resistance, decrease in blood pressure and increased cardiac output and heart rate (Nishimura et al., 1994).

A 0.07 mg/kg medetomidine, 0.3 mg/kg butorphanol and 0.3 mg/kg midazolam protocol has been extensively used in captive suids of multiple species (Morris and Shima, 2003) and is the preferred protocol across suid species at some zoological institutions (Morris et al., 1999). This protocol offers the advantages of being almost entirely reversible and producing consistently good results across species (Morris and Shima, 2003). However, at the doses published, significant bradycardia and hypoxemia are common side effects, and unexplained severe hypoglycemia has been seen in fasted and unfasted suids (Morris and Shima, 2003). Lingering sedation from which suids can be aroused is often seen at high doses using this drug combination for immobilization. Lower doses, as low as 0.04 mg/kg medetomidine, 0.08 mg/kg midazolam and 0.15 mg/kg butorphanol have been used successfully in babirussa, red river hogs, and warthogs, and might be used in other species. These lower ranges were derived from the domestic swine literature (Sakaguchi et al., 1992b; Nishimura et al., 1994), and may reflect variations in individual and species susceptibility. For most pigs, a large volume of induction drugs is needed, although the recent availability of highly concentrated medetomidine,

midazolam, and butorphanol will allow smaller volumes of induction.

Similar variations of this protocol have been described. A combination of butorphanol (0.3–0.4 mg/kg), detomidine (0.06–0.125 mg/kg) and midazolam (0.3–0.4 mg/kg) has been used in Vietnamese potbellied pigs, Eurasian wild boars, red river hogs, warthogs, bearded pigs, and babirussa (Calle and Morris, 1999). This protocol is characterized by rapid, smooth induction with excellent relaxation. In this combination, xylazine (2-3 mg/kg) has been substituted for detomidine and tiletaminezolazepam (0.6 mg/kg) has been substituted for midazolam in some species with similar results (Calle and Morris, 1999). The authors suggest that some species are more sensitive to this drug combination based on temperament (red river hogs, babirussa, and potbellied pigs), and lower dosages of butorphanol can be used. Bearded pigs, warthogs, and Eurasian boars may require the higher end of the suggested dosage range.

These protocols are costly when compared to other options, and a large portion of the cost is associated with the reversal agents (flumazenil, naltrexone, and atipamezole).

Propofol Because propofol must be administered IV, it is an impractical choice for induction of anesthesia in exotic suids. However, propofol can be used as an anesthetic supplement to reach a deeper plane of anesthesia, or used for maintenance of anesthesia. At higher infusion rates, heart rate and cardiac index decrease in domestic pigs (Moon and Smith, 1996). Propofol can be a significant respiratory depressant if administered rapidly, or if high doses are used.

Inhalant Anesthetics The use of inhalant anesthetic gases as induction agents is impractical in most exotic suid species. However, inhalant anesthetics can be used in small or severely debilitated animals, or for maintenance of anesthesia after induction with an injectable agent. Sevoflurane is the safest inhalant anesthetic agent currently available. Minimum alveolar concentrations (MAC) for domestic pigs are estimated at 0.9 to 1.25 for halothane, 1.5 to 2.0 for isoflurane, and 2.0 to 2.7 for sevoflurane (Thurmon et al., 1996). A study done on newborn swine comparing halothane, isoflurane, and sevoflurane showed that mean systemic arterial pressure and heart rate decreased the least with sevoflurane when compared to awake piglets, but heart rate decreased the least with isoflurane (Lerman et al., 1990). Mean measurements of systemic arterial pressure were also lower in isoflurane and halothane-anesthetized piglets than when sevoflurane was used. Sevoflurane is associated with faster recoveries than other inhalants. Caution should be used with domestic pigs known to be susceptible to malignant hyperthermia, as this condition can be triggered by inhalants, and traditionally associated with halothane usage.

Long-Acting Tranquilizers Limited objective information is available on the use of long-acting tranquilizers in suids. Perphenazine, a long-acting phenothiazine, has been used at 30 to 50 mg per warthog prior to translocations (Ebedes, 1993). Two young warthogs overdosed with perphenazine at 5 mg/kg died 3 days later. Although it is unclear if the animals died directly from the overdose, the warthogs did not eat after drug administration (Ebedes, 1993).

CONCLUSIONS

Balanced anesthetic protocols using multiple drug combinations allow for less detrimental side effects with better anesthetic qualities. Clinicians should choose the protocol that is likely to achieve the desired level of anesthesia while balancing against the detrimental effects most likely to be significant for an individual patient.

As newer monitoring equipment becomes available and is applied to document the physiological effects in non-domestic suid anesthetic episodes, the literature should evolve into more scientific and objective descriptions of different anesthetic protocols. Ultimately, this will help in refining techniques applicable to the captive and free-ranging management of these species.

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Hippopotami

Michele Miller

INTRODUCTION

Hippopotamus anesthesia often invokes feelings of dread in both animal care staff and veterinarians because of its difficulty and historically poor success rate. Their large size, limited vascular access, and dive reflex may present tremendous anesthetic challenges. However, improvements in anesthetic agents, equipment, and techniques have increased the number and type of procedures that can be performed on these species.

TAXONOMY AND ANATOMY RELATED TO ANESTHESIA

There are two genera of hippopotamus, each with one species indigenous to Africa. The Nile or common hippopotamus, *Hippopotamus amphibibius*, is frequently exhibited in zoos. The typical adult weight range in captivity is 1,300 to 2,500 kg, with the male being larger than the female (Miller, 2003). Wild adult weight ranges are 1,179 to 2,500 kg for males and 1,185 to 2,300 kg for females. Their nostrils are set on the top of the muzzle and are capable of closing. The skin contains abundant mucous glands that secrete an oily substance that can make handling difficult.

The pygmy hippopotamus, *Choeropsis liberiensis*, is a pig-sized animal restricted to coastal regions of West Africa. Since these animals are forest dwellers, their anatomy is adapted to this environment. The orbits are set midway on the side of the skull instead of high on the head, like the common hippo. The male is usually only slightly larger than the female, with adult weights ranging from 160 to 350 kg.

BIOLOGY AND PHYSIOLOGY

The common hippo is widely distributed in sub-Saharan Africa. They are social animals and found in groups consisting of females with offspring and an older male. In

captivity, common hippos are usually kept as pairs or compatible groups of females. Hippos spend most of the daytime resting in or near the water in order to thermoregulate and exit during the evening to feed. If the animals feel threatened, they may retreat to the water. This behavior is also a concern when attempting capture or immobilization.

Hippo skin plays an important role in thermoregulation and control of water loss. This layer consists of a thin epidermis over a thick dermis. There are large subdermal glands that secrete viscous alkaline secretions that are thought to play a role in wound healing as well as providing evaporative cooling (Eltringham, 1999). The secretions turn brownish-red on exposure to air. During times of excitement, there may also be increased secretion from the skin.

Unlike the larger hippo, the pygmy hippo is a solitary animal except to mate. It forages in the forest between mid-afternoon and midnight, spending the rest of the day in the swamp or river vegetation. Pygmy hippo skin also produces abundant mucous secretions.

VASCULAR ACCESS SITES AND MONITORING

The thick skin of the hippopotamus confounds attempts to obtain diagnostic samples and monitor anesthesia. Visualization of blood vessels is difficult. Methods for localization include using Doppler and ultrasound probes, but dissection shows that most superficial veins are thin-walled and easily collapsed.

A number of venipuncture sites have been used in hippos (Morris, 2001; Miller, 2003). The ventral tail artery, using an approach similar to that for domestic cattle, can provide a reasonable volume of blood. Lateral tail veins are less reliably found. Cephalic, median (found on the medial aspect of the antebrachium) (Figure 50.1), and palmar digital (found on the caudal aspect of the lower limb) veins can be used for blood collection and intravenous (IV) injections, but may be



Figure 50.1. Post-mortem dissection of the cephalic vein in a hippopotamus.

difficult to find in adult animals. On the hindlimb, medial saphenous and plantar digital veins are sometimes accessible (Figure 50.2). For small volumes, the auricular veins can be used, but these are easily collapsed or injected perivascularly. In smaller individuals, blood can be collected from the vena cava using a technique similar to that used in domestic swine. In most cases, venipuncture in hippos will be a blind attempt based on anatomical landmarks rather than visualization of actual vessels.

IV catheterization has been attempted and is almost universally unrewarding because of the thickness of the surrounding skin. Cut-down techniques have also been tried in a juvenile hippo as well as intraosseous catheterization with a large-gauge spinal needle (Miller, unpublished results). This may be useful for fluid and/or drug administration in critically ill juvenile hippos with limited mobility.

Simple auscultation of hippos is also thwarted by their large size and thick skin. Typical parameters for anesthetic monitoring should also be applied to hippos,



Figure 50.2. Post-mortem dissection showing anatomy of the superficial veins on the medial surface of a hippopotamus's hind leg.

including temperature, heart rate and rhythm, respiratory rate, depth, and oxygen saturation.

Temperature regulation during immobilization is important, especially for prolonged procedures or those performed in warm ambient conditions. Water should be available to aid cooling by keeping the skin moist and provide an enema if necessary. Rectal temperature can be measured using a large animal thermometer but is more accurate if a digital thermometer with long probe is available. In several cases, readings were 34.4°C to 37.2°C (Ramsay, 1998; Morris, 2001). The probe should rest against the rectal mucosa for the best reading and can be taped to a large syringe case to ensure placement.

The new electronic stethoscopes can facilitate monitoring in smaller individuals, but size and positioning in adults may make this method of monitoring heart rate and respiratory sounds difficult. A Doppler ultrasound probe can be placed directly on the cornea or sometimes over superficial palmar/plantar digital arteries to provide an audible measure of heart rate. Heart rates measured under various anesthetics ranged between 20 and 60 beats/minute (bpm) (Ramsay, 1998; Weber, personal communication). Pulse oximeter probes must be placed in thinly skinned areas, such as the inside of a lip, eyelid, frenulum, pinna, rectum, vulva, or prepuce in order to measure heart rate. Oxygen saturation readings from these probes should be critically evaluated since peripheral vasoconstriction, skin pigmentation and thickness, and other factors may lead to inaccurate readings. Hypoxemia is common and readings may be as low as 55% to 79% (Ramsay, 1998). However, values greater than 85% were obtained when hippos were supplemented with oxygen (Miller, unpublished results) (Figure 50.3). Electrocardiography is not typically used except in smaller individuals. Leads should be attached to percutaneous needles to allow adequate transdermal conduction of the signal, and then should be employed as a heart rate and rhythm monitor only.



Figure 50.3. Nasal insufflation of oxygen in an immobilized hippopotamus.

Direct visualization of thoracic excursions, movement of the rebreathing bag on the anesthetic machine, and auscultation in smaller individuals are methods of measuring respiratory rate in hippos. Respiratory rates are typically 3 to 30 breaths/minute (Ramsay, 1998; Miller, unpublished results). A capnograph or respirometer can be used if the animal has been intubated and provides information on adequate ventilation as well as respiratory rate. Blood gas values have been published on an immobilized juvenile pygmy hippo (Morris, 2001).

INTUBATION

Intubation of anesthetized hippos is recommended for any prolonged anesthetic procedure. However, positioning and the weight of the hippo's head can make intubation difficult, especially in adult common hippos. Equipment should be available to assist in repositioning the head as well as safely keeping the mouth open (mouth gag). Items that have been used include noosed poles, ropes, and wooden boards with center holes for arm insertion. The fleshy tongue, redundant jowls, and long soft palate can obscure direct visualization of the glottis. These structures can be pushed out of view by a long laryngoscope blade or hand, or intubation can be performed by palpation of the epiglottis. A 24- to 30-mm endotracheal tube is required for an adult common hippo (Morris, 2001). Because of the pygmy hippo's narrower caudal pharynx and smaller trachea, intubation is a more difficult procedure and usually is accomplished by blind manual palpation (Weston, 1996; Flach, 1998). A 14-mm endotracheal tube is an appropriate size for intubation in the adult pygmy hippo (Flach, 1998).

REVIEW OF REPORTS ON HIPPO IMMOBILIZATION AND ANESTHESIA

There is a paucity of anesthetic reports in the literature. Many of the earlier citations are descriptions of problems associated with dealing with immobilizations or capture (Van Niekerk, 1962; Pienaar, 1967).

Historically, narcotic anesthetic agents have been used most commonly to immobilize hippos. Usually this involved etorphine (M99) alone or combined with a sedative such as xylazine or acepromazine (Stoskopf, 1978; Pearce, 1985; Ramsay, 1998; Loomis, 1999). Complications were common, including apnea, cyanosis, bradycardia, and fatal cardiorespiratory arrest. In a review of 16 immobilizations of adult Nile hippos using etorpine with or without xylazine or acepromazine, 10 were performed without complications (Ramsay, 1998). Accurate weights are often difficult to obtain so most drug dosages are estimated. In this report, etorphine was used at a total dose of 2 to 6 mg/animal IM, resulting in an estimated dosage of 1 to 5 μg/kg. Xylazine was added with the initial etorpine administration in six procedures at 100 mg total dose (estimated 67-83 ug/kg). Etorpine was combined with 22 mg acetylpromazine (22 µg/kg) in one case. Drug effects similar to other ungulates were observed in hippos with the mean time to initial sedation occurring at 12 minutes and recumbency in 31 minutes. Nasal insufflation with oxygen or intubation with intermittent positive pressure ventilation appeared to improve oxygen saturation values in two hippos in which these procedures were performed. Respiratory complications were successfully treated with doxapram in three of four hippos. The remaining hippo died despite administration of reversal agents. Thirteen hippos were reversed with diprenorphine (M50-50) at two to three times the total etorphine dose, and two also received naltrexone at 100 times the etorphine dose. Two cases that received xylazine were also given yohimbine.

Fewer published reports exist on anesthesia in the pygmy hippo. A summary of 21 anesthetic events on a single adult female (216 kg) requiring ongoing treatment provides interesting comparisons of several drug combinations for this species (Pearce, 1985). Xylazine (1.4 mg/kg IM), followed by ketamine (5–8 mg/kg IM), induced recumbency and provided adequate restraint for minor handling, although the animal was arousable. For more invasive procedures or those requiring better restraint, it was recommended that 100 to 150 mg xylazine combined with 2 to 3 mg etorphine be used in an adult pygmy hippo (Flach, 1998). Excitement, muscle rigidity, and increased salivation were observed during induction with etorphine alone, but seemed to be reduced when xylazine was added. Higher doses of

etorphine did correspond with increased periods of apnea (Flach, 1998). Ketamine has been given following etorphine and xylazine to further relax a pygmy hippo for intubation (Flach, 1998). This animal underwent a Caesarian section and had to be manually ventilated (Flach, 1998). The heart rate varied between 42 and 100 bpm and the respiratory rate was between 0 and 10 breaths/minute (Flach, 1998).

The high fatality rate for these species often cited in the literature may be partially resulting from the historically quoted high doses (4–12 mg etorphine \pm 1 mg/kg xylazine) and use of etorphine as a sole agent (Taylor, 1986). The ability to train animals to enter restraint devices, obtain accurate weights on hippos, along with improvements in drug delivery systems, and availability of newer more potent, selective, and reversible anesthetic agents have increased the number and success of hippo anesthetic procedures in recent years.

More recently, a series of 10 cases have been reported using a combination of detomidine and butorphanol to produce profound sedation in juvenile common hippos (Morris, 2001). Although animals could be aroused with sufficient stimulation, this drug combination appeared to be adequate for most noninvasive procedures such as examinations and blood collection. Supplemental ketamine (1 mg/kg IV) provided additional restraint in three cases. Nasal insufflation or intubation and assisted ventilation with oxygen improved oxygen saturation.

Hippos were darted with a combination of detomidine (0.05 mg/kg) and butorphanol (0.15 mg/kg) IM. Effects were reversed using yohimbine at 0.3 mg/kg with naltrexone at 0.5 mg/kg or atimpamezole at 5 mg per 1 mg detomidine with naltrexone at 0.5 mg/kg IM. No cases of recurrent sedation were observed with this combination.

Various modifications of this combination have been published in the literature for induction or as the sole restraint agent for examination or other procedures in hippos (Clyde, 1998; Dumonceaux, 2000). Detomidine and butorphanol have also been used in pygmy hippos. In one adult male pygmy hippo, detomidine (44 μ g/kg) was administered orally with diazepam (0.5 mg/kg) as a preanesthetic sedative (Weston, 1996). A combination of ketamine, detomidine, and butorphanol was used to induce and isoflurane used to maintain general anesthesia for surgery. Although only yohimbine was used as a reversal agent (0.11 mg/kg IM), the hippo was standing within minutes.

STRATEGIES FOR FIELD CAPTURE AND ANESTHESIA IN REMOTE LOCATIONS

Immobilizing hippos in field conditions or remote locations compounds the difficulties of anesthesia in these species. It is imperative to prevent access to water for successful capture using either physical or chemical methods. Hippos can drown in pools with

water greater than 15 cm in depth (Maritz, 2001). Therefore, trapping of hippos is still the preferred technique for field capture.

Physical capture usually requires construction of a capture boma with a funnel leading from the pool containing the hippos to be captured. Electric fencing can be placed around the pool but sturdy panels, without horizontal footholds, should be used for the boma wall and trap door. Feeding inside the capture boma should occur for several days to weeks prior to capture. A passageway with sliding doors should lead from the boma to the transport vehicle. Azaperone has been used for transporting aggressive hippos (Maritz, 2001). General doses are 400 mg for an adult bull, 300 mg adult cow, 200 mg sub-adult, and 100 mg for a yearling.

A modification of this technique can be used for chemical capture of hippos. All equipment and personnel should be in place prior to the capture event to minimize the risks to animals and staff. Etorphine is the drug used in most field immobilizations. General doses are based on the condition of the animal but guidelines for maximum amounts are 2.5 mg for an adult bull, 2 mg adult cow, 1 mg sub-adult, and 0.2 mg for a yearling (Maritz, 2001). All animals in the boma are darted, or released once the animals are immobilized. The anesthetized hippo should be moved onto a sled and winched onto the transport vehicle, then reversed.

GUIDELINES FOR ANESTHESIA IN HIPPOPOTAMUS

Immobilization Planning and Preparations

Generally, the events requiring anesthesia in captive hippos are known ahead of time so that staff and equipment can be prepared in advance. Preparations should include securing an area that prevents the hippo's access to water and moats during the anesthetic induction and recovery periods. Equipment should also be acquired and positioned that can move the animal if it falls in a compromised position, such as a forklift, crane, or winch with a skid and heavy loading straps. Padding is desirable for long procedures to prevent pressure on dependent structures such as head and limbs. Partially inflated truck inner tubes work well as cushions.

Hyperthermia can be a concern because of the insulating subcutaneous fat layer. Ideally, procedures should be planned for the coolest part of the day. Ice, water, and a hose should be available. Regular temperature monitoring and prevention of hyperthermia or hypothermia in small individuals is critical.

Most hippos are fasted for 24 to 48 hours prior to anesthesia (Loomis, 1999). This may prevent regurgitation but also decrease the weight of gut contents on the diaphragm during recumbency. Hippos have slower gastrointestinal transit times than other herbivores with

retention of food in the stomach from up to two nights of feeding (Eltringham, 1999). Water intake should also be restricted for 12 to 24 hours.

Induction

The most common sites for drug injection are in the neck just behind the ear, but can also be in the caudomedial thigh. Intramuscular injection requires a needle length of 60 to 64 mm in an adult hippo. Induction time may vary significantly depending on the degree of subcutaneous injection. Depending on the drug used, initial signs vary, but hippos may show ataxia, vocalize, and have increased sweating and salivation. They often "dog sit" prior to becoming recumbent. If the procedure is non-invasive, requires only mild restraint, or is being performed in protected contact, it may be feasible to start at this point. Even when a hippo becomes recumbent, especially when using non-etorphine regimens, the hippo can be aroused with stimulation and staff should be prepared to exit to a safe location.

Nile Hippo Anesthetic Regimens

In some cases, procedures may require only mild sedation, especially if hippos have been trained and a restraint device is available. Azaperone has been used at a total dose of 400 to 800 mg IM in adult hippos for procedures such as wound treatment (Kruger, 1996). Oral acepromazine (0.2 mg/kg) provided mild sedation for a juvenile hippo during transport (Miller, 2003).

Detomidine-butorphanol has been used for minor procedures or as induction agents for general anesthesia. The dosages are 0.02 to 0.06 mg/kg detomidine with 0.06 to 0.20 mg/kg butorphanol IM, administered in the same dart. For example, a 2,270-kg hippo was induced using 100 mg detomidine with 300 mg butorphanol IM (Dumonceaux, 2000). This provided adequate restraint 22 minutes after darting to intubate and prepare for surgery. Another adult female hippo (estimated weight 950 kg) was sedated with 40 mg detomidine and 60 mg butorphanol IM in a chute for skin biopsy and blood collection (Clyde, 1998). The author prefers to use a 3:1 ratio of butorphanol:detomidine with starting dosages of approximately 0.15 and 0.05 mg/kg IM, respectively. Supplemental doses of this combination can also be used to increase the level of sedation. Onset of effects varies, but initial signs may be seen at 10 to 20 minutes with recumbency at 20 to 30 minutes. However, longer times have been observed, especially if partial administration or subcutaneous injection occurs.

Anesthesia can be maintained by providing isoflurane via face mask, nasal tube, or endotracheal tube. Flow rates of up to 15 L/minute may be required, so ideally a large animal anesthetic machine should be used. Intermittent positive pressure ventilation at rates of 5 breaths/minute can be used to improve oxygen saturation and deliver anesthetic gas.

If a portable anesthetic vaporizer is not available, injectable anesthetic agents can also be used to maintain anesthesia. These include incremental doses of butorphanol-detomidine, ketamine, and etorphine (Morris, 2001; Miller, 2003). Propofol administered at 50 to 100 μ g/kg per minute could also be used if venous access was established (Morris, 2001). Rapid reversal of effect seen with this drug could be dangerous in this species so it should only be considered in combination with other anesthetic agents.

Reversal of detomidine-butorphanol is accomplished by administration of naltrexone at 0.4 to 0.6 mg/kg IM and either yohimbine at 0.1 to 0.3 mg/kg IM or IV, or atipamezole 5 mg IM for every 1 mg detomidine. Signs of arousal are usually rapid unless the animal has received other supplemental drugs.

Alternative anesthetic protocols include ketamine-medetomidine for induction. IM medetomidine (40 mg) and ketamine (900 mg) successfully anesthetized a 600-kg hippo; 50 mg atipamezole was used for reversal (Klarenbeek, personal communication). However, a second hippo, 700 kg, died secondary to apnea after administration of 45 mg medetomidine and 1,000 mg ketamine IM.

Etorphine at 0.001 to 0.005 mg/kg (or 2–6 mg total dose) with or without xylazine at 0.067 to 0.083 mg/kg (100–150 total dose) IM can also be used for general anesthesia in hippos. Reversal can be achieved with naltrexone at 100 times the etorphine dose IM and yohimbine at 0.1 to 0.3 mg/kg IM. Complications with apnea, bradycardia, and hypotension can occur and the veterinarian should be prepared to administer supplemental oxygen and doxapram as needed. If adverse signs are significant, consideration should be given for complete reversal.

Pygmy Hippo Anesthetic Regimens

Similar to their larger counterparts, there are occasions in which the pygmy hippo may require only sedation or short periods of restraint for tusk work or wound care. Ketamine at 1 mg/kg has been used successfully to immobilize pygmy hippos for short periods (Morris, 2001). Midazolam (0.1 mg/kg) has also been used as a mild sedative or for muscle relaxation in conjunction with other anesthetic drugs in pygmy hippos (Mehren, personal communication).

Experience with detomidine-butorphanol combinations is not as extensive in pygmy hippos. The ratio of detomidine to butorphanol is slightly different at 1 to 5, with dosages of 0.04 to 0.06 mg/kg and 0.1 to 0.2 mg/kg IM, respectively (Morris, personal communication). Reversal agents are used in the same way as those for common hippos with this combination.

Another combination that has shown promise is medetomidine-butorphanol. The dosage used was 0.2 mg/kg butorphanol and 0.036 mg/kg medetomidine IM (Morris, personal communication). This was reversed

with atipamezole and naltrexone. Similar to the effect in common hippos, both α_2 -agonist-butorphanol combinations could result in an animal that was able to be aroused with stimulation.

Etorphine (2–3 mg) combined with xylazine (100–150 mg) can be used to induce and maintain general anesthesia in pygmy hippos. The same complications with narcotics are observed in this species as seen with common hippos. Reversal with yohimbine or atipamezole and naltrexone is described above.

Recovery

Once the procedure has been completed, the hippo should ideally be positioned so that it will not be traumatized or fall into a compromised position during recovery. Moving the patient is not always practical but providing good footing and removing obstacles should be the goal. Reversal agents should be administered only after staff and equipment have been moved to a safe area. If possible, rolling the hippo to sternal recumbency may aid it in standing. Warn staff and know emergency escape routes since this may arouse the animal sufficiently to stand or move its head. The hippo should be monitored until capable of ambulating safely before being left unattended. If the hippo is arousable but requires additional reversal agents, these should be administered by dart to minimize risk to staff.

Hay and access to drinking water can be provided once the animal is alert and walking steadily. Because of the risk of re-narcotization, access to a pool should be withheld for at least 24 hours, especially when using narcotics. A mister or sprinkler system should be used to keep the animal comfortable in the absence of a pool during this time.

Anesthetic Records

Accurate records of drugs used, effects, complications, and physiological data are critical for evaluation of the anesthetic event as well as improvement of future anesthetic protocols. During planning, one person should be assigned as the record-keeper to record all relevant details. A debriefing is also a valuable part of the procedure and can reveal important details that may have been overlooked.

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Camelids

Khursheed R. Mama

INTRODUCTION

Anesthesia may be required for diagnostic and corrective procedures in veterinary hospitals, zoological parks, in the field, or in the animal's natural habitat. This chapter attempts to provide information relevant to anesthetic management of camelids so as to maximize chances of a favorable outcome.

It is important to recognize that camelids are native to very different geographical areas, ranging from the high altitude of the Andes to deserts of India, Africa, and the Middle East. As such even though they are all camelids, their physiological adaptations differ. For example, camels are well adapted to drought conditions and may store and draw on water reserves. Llamas and alpacas have a left-shifted oxygen hemoglobin dissociation curve and their red blood cell configuration and hemoglobin content differ from many other mammalian species (Chiodi, 1970; Fowler et al., 1989a; Van Houton et al., 1992). These are likely adaptations for survival at high altitudes where the oxygen tension is low.

PATIENT RESTRAINT AND HANDLING

Fasting prior to general anesthesia is recommended to minimize regurgitation, aspiration, and bloating. Depending on the nature of the procedure and anticipated duration of recumbency, a 12- to 18-hour fasting period is recommended in adult llamas and alpacas; a 24- to 36-hour fast has been recommended for camels. Many recommend withholding water in addition to feed for at least a portion of that time. Fasting of nursing juveniles is not necessary and may increase their stress and likelihood of metabolic derangement.

Camelids may be trained to a halter and led using this. A towel may be hung loosely over the nostrils and mouth in the event that an animal attempts to spit at the handler. A small corral may be used to facilitate catching an individual animal from a herd. An arm placed around the neck of llamas and alpacas will help restrain the patient until a halter can be placed. Chutes designed especially for llamas and alpacas greatly facilitate restraint for procedures such as catheter placement. Domesticated camels may be restrained in stocks designed for horses or eased to sternal recumbency using a rope placed around the forelimb. They may also be trained to a seated (cushed) position by their handler.

INSTRUMENTATION

Intravenous catheterization and endotracheal intubation have historically been considered challenging in camelids. Success can be maximized with proper knowledge of the anatomy and availability of appropriate equipment.

The most common site for venous access in camelids is the jugular vein. The greatest challenge in placing a jugular catheter in adult camelids is lack of animal compliance. Many patients "cush" and rise during the procedure, creating a moving target. Restraint in an appropriate chute or stanchion can help significantly. The other difficulty faced when placing a jugular catheter is locating the vein. Many camelids, especially males, have thick (up to 1-in.) skin in the proximal portion of their neck and balloting the vein can prove challenging, especially as the vein is fairly deeply located. Therefore, knowledge of the anatomical landmarks is important. In the proximal neck the jugular vein is located at the bisection of a line drawn caudally from the lower jaw with a line drawn ventrally from the base of the ear (Davis et al., 1996). Despite difficulty palpating the vessel in the proximal portion of the neck, many prefer this site for catheter placement because of better separation between the jugular vein and carotid artery (Davis et al., 1996; Riebold et al., 1989). Distention of the vein is best accomplished by holding off behind the palpable ventral projection of the C6 vertebra. If one is still unable to palpate the vein, a narrow gauge

(25- or 23-) inch-to-inch and a half needle may be used to locate the same prior to catheter placement.

Once the vein is located and the site appropriately prepared, an incision through all the layers of the skin is recommended in the adult camelid. This incision is best made with a scalpel blade after subcutaneous local anesthetic (1–2 ml of 2% lidocaine) is infiltrated at the site (Heath, 1989). In order not to accidentally lacerate the vessel, do not distend the vein while making this incision through which the catheter may then be placed. Continue to distend the vein while the catheter is advanced to minimize the chance of it getting caught on valves within the same. Valves have been anecdotally reported to impede threading the jugular catheter. Secure the catheter so that it does not kink at the point of entry through the skin (Figures 51.1, 51.2, and 51.3).

Alternate sites for catheter placement include the lateral thoracic vein in adult camels and the cephalic or



Figure 51.1. Placing a jugular catheter in a llama.



Figure 51.2. Suturing a jugular catheter after placement in a llama.

saphenous vein in juvenile patients. Auricular vessels may be used in anesthetized patients. The size of the catheter used should be appropriate for the size of animal with consideration given to the reason for its placement. For example, a large gauge catheter similar to that placed in adult patients is generally unnecessary in a 10-kg cria. Alternatively, if significant hypotension is expected in an adult patient because of the disease process or anticipated hemorrhage, at least one large-gauge catheter is recommended.

The technique for endotracheal intubation varies with the camelid species in question. For llamas and alpacas, visual orotracheal intubation is facilitated by appropriate equipment and positioning. Ideally the animal should be placed in sternal recumbency with the head extended. A ruminant mouth gag or strips of tape or gauze may be used to spread the jaws and facilitate visualization using a long but narrow laryngoscope blade (Figure 51.4). Intubation may be performed directly using an endotracheal tube or either directly or retrograde by first placing a flexible guide to help direct the endotracheal tube into the trachea (Sanchez et al., 1993). Topical local anesthetic (lidocaine) is used to facilitate intubation in the lightly anesthetized patient. The tube is generally secured behind the ears after the cuff is inflated (Figure 51.5). Passage of the tube via the nasal passage (nasotracheal intubation) may also be performed in llamas and alpacas (Riebold et al., 1994). The tube is passed into the trachea via the ventral medial nasal meatus after proper lubrication. Although this

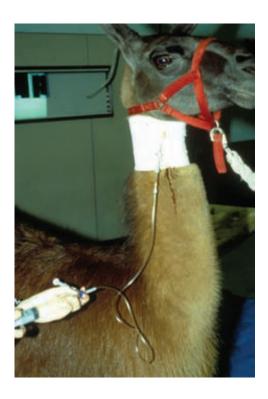


Figure 51.3. Anesthetic induction drugs being given intravenously through a jugular catheter.

usually necessitates a smaller tube (e.g., 8- or 9-mm internal diameter vs. 12- or 14-mm internal diameter in an adult llama) than via the oral route and there is a potential for hemorrhage during placement, the tube may be left in place until the animal is fully recovered without fear of the patient chewing it. Vasoconstrictors such as phenylephrine may be administered topically to minimize hemorrhage during nasotracheal tube placement. Because camelids are nasal breathers, this method helps minimize the risk of upper airway obstruction in the recovery period. This technique may also be used to minimize the need to work around the endotracheal tube during procedures involving the oral cavity.

In adult camels intubation is usually performed blindly or by manual palpation of the arytenoid



Figure 51.4. Endotracheal intubation in the llama using a flexible stylet.



Figure 51.5. Intubated llama under general anesthesia.

cartilages. After the patient is adequately anesthetized a large animal mouth gag may be used to facilitate introduction of the arm into the oral cavity. If the oral cavity is too narrow, a guide tube may first be inserted into the trachea. Caution must be exercised to prevent laceration of the endotracheal tube on the rear teeth. Depending on the size of the patient, a range of tubes from 16 to 26 mm internal diameter may be necessary (Alsobayil et al., 1999).

ANESTHETIC TECHNIQUES

Regional and general anesthetic techniques may be used in camelids. General anesthesia may be achieved with injectable agents, inhaled agents, or a combination of these. For the reader who wishes to pursue this further, detailed reviews of anesthetic drugs and techniques for camelids are available (Fowler, 1989b; Alsobayil et al., 1999; Mama, 2000a). Regardless of the drugs selected, keep in mind that the range of body weights is very broad among camelids, ranging from an 8- to 10-kg newborn cria to a 500-kg camel; consequently, it is important to try to get an accurate weight and calculate dosage based on this. Fiber in adult llamas and alpacas can be very misleading, and when a scale is not available, palpation of the patient may assist in determining weight. Typically adult alpacas weigh 40 to 60 kg, whereas body weight in adult llamas may range from 120 to 300 kg. Body weight also influences equipment requirements ranging from endotracheal tubes and the anesthetic machine to the type of padding used.

Regional Anesthesia

Regional administration of local anesthetics can facilitate surgical intervention and minimize the need for administration of drugs with systemic effects. Local anesthetics may be used to facilitate a host of procedures. Blocking individual nerves (e.g., the mandibular nerve for dental procedures involving the lower jaw) are commonly used as an adjunct to general anesthesia. However, some regional techniques may also be used in the awake or sedated patient.

For example, paravertebral blocks similar to those described in both horses and cattle have been used in camelids (Said, 1964; Fowler, 1989b). Epidural techniques are also described. Caudal epidural administration of 12 to 15 ml of 2% lidocaine in a sternally recumbent adult camel provides anesthesia of the perineum and udder or scrotum for 1 to 2 hours without influencing motor control (White, 1986a). Lidocaine (0.22 mg/kg) and xylazine (0.17 mg/kg) have been used to facilitate diagnostic and surgical procedures involving the rectum, vagina, and perineum in llamas (Grubb et al., 1993). The onset of anesthesia was 3 to 4 minutes following either lidocaine or xylazine and lidocaine, but the duration varied significantly, lasting about 1 hour in the lidocaine group and 6 hours in the group receiving

both drugs. Analgesia following xylazine alone was evident after about 20 minutes and lasted 3 hours. Mild sedation is reported in animals receiving xylazine. Epidural morphine at doses similar to those used in other species may provide longer-term analgesia and may have value for post-operative analgesia for procedures involving the hind limbs or caudal abdomen and perineum.

Drugs for Sedation and Field Anesthesia in Domesticated Camelids

Many techniques and drugs for sedation and anesthesia have been used in camelids. For detailed information on the same and individual drug effects, the reader is referred to more comprehensive reviews and references therein (Fowler, 1989b; Alsobayil et al., 1999; Mama, 2000a). This section highlights commonly used techniques for domesticated animals.

Intramuscular (IM) and intravenous (IV) administration of xylazine or xylazine and ketamine have been extensively described for use in llamas, alpacas, and camels (White et al., 1987; Gavier et al., 1988; Fowler, 1989b; Bolbol, 1991). Although these drugs alone and in combination do provide effects ranging from sedation to short-term anesthesia, the degree (level of sedation or anesthesia) and duration (range, 10-60 minutes of response in individual animals) is variable. The addition of butorphanol to an IM combination of xylazine and ketamine has also been evaluated in llamas and alpacas. Xylazine, butorphanol, and ketamine all IM were administered to seven male llamas and seven male alpacas based on dose recommendations from Dr. LaRue Johnson (Mama et al., 2000b) (Table 51.1). Most animals became recumbent in an average of 4.3 (llamas) and 6.7 (alpacas) minutes. Induction quality was good, with animals generally showing some degree of ataxia before assuming a sternal or lateral position. Despite receiving lower drug doses, llamas appeared more deeply anesthetized and remained recumbent for a longer duration (mean time to standing 63 minutes) than did alpacas (mean time to standing 22 minutes). All animals recovered without apparent complications, but hypoxemia (average PaO₂ 45-55 mmHg), barometric pressure (640 mmHg) and mild hypoventilation (average PaCO₂ 46-49 mmHg), associated with recumbency was commonly seen in this study. Direct mean auricular arterial blood pressure was well maintained, averaging 131 mmHg in llamas and 144 mmHg in alpacas; heart rate ranged from 29 to 37 beats per minute (bpm) in llamas and 37 to 49 bpm in alpacas.

Other α_2 or dissociative and/or benzodiazepine combinations include xylazine and tiletamine/zolazepam or medetomidine and ketamine (Waldridge et al., 1997; Hammer et al., 1999; Dubois et al., 2004). Selection of a specific α_2 or dissociative agent is in large part based on drug availability, circumstance, and familiarity on the part of the veterinarian. Effects may vary in duration and magnitude but tend to be similar among the different agents.

Butorphanol (0.1 mg/kg, IM) has also been used in combination with intra-testicular lidocaine (2%, 2–5 ml per testicle) for chemical restraint to facilitate standing castration in over 100 llamas (Barrington et al., 1993). The authors' impression was that the animals receiving butorphanol appeared less stressed than those receiving only intra-testicular lidocaine.

Similar drug combinations are used for anesthesia in field conditions for camels. White et al. (1987) described the use of intramuscular xylazine and ketamine individually and in combination. Behavioral responses and measured cardiovascular parameters of the combination were thought to be improved over individually administered drug. Detomidine and medetomidine have also been used alone to provide sedation or in combination with ketamine for anesthesia. The effects of the α_2 drugs may be reversed with yohimbine or atipamezole at the conclusion of the procedure to facilitate a more rapid recovery (Riebold et al., 1986; Waldridge et al., 1997). Although tolazoline has also been used for reversal of α_2 effects, there is some concern about complications following its administration in camelids.

The phenothiazine tranquilizers are a class of drug that seem to be more widely used in camels than in llamas and alpacas. Although acepromazine is the tranquilizer most veterinarians are familiar with, other drugs in this class include propionyl promazine, chlorpromazine, and triflupromazine. These drugs tend to have prolonged effects and are not reversible, but in most circumstances animals are quieted and seem generally less responsive to their surroundings (Alsobayil, 1999).

Drugs for Sedation and Field Anesthesia in Non-domesticated Camelids

Many of the aforementioned techniques may be used at modified dosages to provide chemical restraint for nondomesticated camelids. For example, Sarno et al. (1996) reported on the use of tiletamine and zolazepam for immobilization of guanacos in a Chilean national park. However, other drugs may also be used in this circumstance. Potent opioids such as etorphine have been used in camels either alone or in combination with acepromazine, ketamine, xylazine, detomidine, or butorphanol (deMaar et al., 1998; Blumer et al., 1999; Walzer et al., 2006). Pacing is commonly described prior to recumbency when potent opioids are used without a tranquilizer. Significant respiratory depression is a potential complication. Therefore, availability of a mechanical breathing device and oxygen supplementation are highly recommended when potent opioids are used. Both the α_2 agent and opioid may be reversed at the conclusion of the procedure.

Anesthetic Techniques for a Hospital Environment

Anesthetic Induction The hospital setting provides a more controlled environment and allows one to better

Table 51.1. Drug protocols for sedation and anesthesia in domesticated healthy adult camelids^a.

Drug or Drug Combination	Dose (mg/kg) and Route of Administration	Approximate Onset (min) of Action and Anticipated End Point	Approximate Duration of Anesthetic Action	Anticipated Recovery for Drugs Resulting in General Anesthesia
Sedation Acepromazine Xylazine	0.05–0.1, IM 0.25, IM 0.1–0.2, IV	5–15, tranquilization 15, sedation 5, sedation	1–4 hours 1–4 hours 1–4 hours	n/a n/a n/a
ANESTHESIA Xylazine Ketamine	0.1–0.2, IM 2–3, IM	5–10, recumbency	10–20 minutes	45 min to 2 hours
Xylazine Butorphanol Ketamine	0.03-0.05, IM 0.3-0.5, IM 2-4, IM	5–10, recumbency	10–20 minutes	20 min to 1 hour
Xylazine Guaifenesin Ketamine	0.1–0.2, IM 50–100, IV 1–2, IV	45 sec after guaifenesin and ketamine, recumbency	10–20 minutes	45 min to 2 hours
Xylazine Diazepam Ketamine	0.1–0.2, IM 0.1–0.25, IV 1–2, IV	45 sec after diazepam and ketamine, recumbency	10–20 minutes	45 min to 2 hours
Xylazine Diazepam Propofol	0.1–0.25, IV 0.25, IV 2, IV	1 minute after propofol, recumbency	10–20 minutes	45 min to 2 hours
Maintenance				
Halothane	Vaporizer set between 0.8%–1.5%	Administered to effect	Administered to effect	30 to 90 minutes following discontinuation
Isoflurane	Vaporizer set between 1%–2%	Administered to effect	Administered to effect	20 to 60 minutes following discontinuation
Sevoflurane	Vaporizer set between 2%–3%	Administered to effect	Administered to effect	20 to 60 minutes following discontinuation
	Drug Protocols for S	Sedation and Anesthesia in Do	omesticated Neonatal Can	nelids*
SEDATION				
Butorphanol Diazepam	0.05–0.1, IV 0.05–0.2, IV	30 sec-1 min 30 sec-1 min	10–20 min 10–20 min	n/a n/a
ANESTHESIA				
Isoflurane	1–3% by mask, to recumbency	Variable but within 5 minutes	While being administered	15–30 min after discontinuation
Sevoflurane	2–4% by mask, to recumbency	Variable but within 5 minutes	While being administered	15–30 min after discontinuation
Diazepam Ketamine Diazepam	0.05–0.1, IV 1–2, IV 0.05–0.1, IV	30–45 seconds after administration 30–45 seconds after	10-20 min	30 min
Propofol	1–2, IV	administration	5-15 min	20-30 min

^aDosages are approximate and may need adjustment for the individual patient and scenario.

titrate drugs to achieve sedation or short-term anesthesia, or to transition a patient to inhalation anesthesia. The placement of an IV catheter facilitates this titration of the drugs to a given end point for an individual patient.

Most induction combinations include either ketamine (2–5 mg/kg titrated to effect) or propofol (2 mg/kg titrated to effect) in conjunction with a centrally acting muscle relaxant such as guaifenesin (25–75 mg/kg), diazepam, or midazolam (0.02–0.1 mg/kg). α_2 -Agonists such as xylazine and medetomidine may also be used, especially in larger and more unruly animals. These may be administered IM to facilitate catheterization or IV prior to ketamine or propofol. Keep in mind that the

dose for xylazine in camelids is between that reported for cattle (0.03–0.1 mg/kg) and horses (0.3–1.0 mg/kg).

Ketamine combinations have been routinely used for anesthetic induction in camelids. Typically animals become recumbent about 45 seconds following IV administration and intubation conditions are good in most circumstances if one is fairly efficient. Additional drug may be safely administered if the patient maintains pharyngeal tone or is swallowing. Although propofol combinations are not used as frequently, studies do report its safety and efficacy in camelids. For example, propofol was used in camels premedicated with xylazine and diazepam to induce and maintain

short-term anesthesia (Fahmy et al., 1995). The same dose has also been used for induction in llamas (Duke et al., 1997).

Inhalation anesthetic induction has been successfully used in llamas and alpacas on occasions in which intravenous catheterization prior to anesthetic induction has proved challenging. Although regurgitation and aspiration concerns are valid, fasted animals are less likely to manifest these complications. However, this process can be quite time consuming; anesthetic induction was reported to take an average of 17 to 19 minutes from time of first isoflurane breath to orotracheal intubation inunpremedicated healthy adult llamas (Mama et al., 1999, 2001). This time may be significantly reduced in debilitated patients and those receiving premedication.

Anesthetic Maintenance When available, inhalation anesthetic techniques are used to maintain anesthesia in patients undergoing highly invasive surgical procedures (e.g., celiotomy, fracture repair, etc.). Halothane, isoflurane, and sevoflurane have all been used to maintain anesthesia in camelids, but studies are limited. One report provides the minimum alveolar concentration (MAC) of isoflurane in llamas $1.05\% \pm 0.17\%$ (Mama et al., 1999), whereas another provides the same information for sevoflurane in both llamas (2.29% \pm 0.14%) and alpacas (2.33% \pm 0.09%) (Grubb et al., 2003). These values are similar to those reported in other species and one presumes that adult camels are similar. A small animal anesthetic machine and breathing circuit are appropriate for llamas and alpacas, whereas a large animal breathing circuit is necessary for adult camels.

Cardiopulmonary and behavioral responses are described with inhalation agents in anesthetized camelids. In adult llamas a decrease in mean arterial blood pressure and an increase in heart rate were observed with increasing isoflurane dose during both spontaneous and controlled ventilation. Cardiac output and PaCO₂ were higher during spontaneous ventilation than during controlled ventilation (Mama et al., 2001). The broadest base of experience in camels is with halothane. Following anesthetic induction with injectable agents, anesthesia has been successfully maintained with halothane vaporizer settings between 1% and 3% (White et al., 1986b; Singh et al., 1994). Blood pressure is reported to be in the same range as for other domestic species, but with a tendency toward higher values much like those observed in cattle. Rapid shallow breaths and rising PaCO₂ values are also described. During inhalation-induced recumbency, spontaneous behaviors (e.g., swallowing, limb movement) decreased with increasing anesthetic depth. Jaw tone and palpebral reflex activity also decreased as isoflurane dose increased. Recovery from anesthesia was also reported to be uneventful (White et al., 1986b; Singh et al., 1994; Mama et al., 1999, 2001).

Inhalation anesthetics are the mainstay for anesthetic maintenance, but the need for specialized

delivery equipment generally limits the use of this technique to the hospital environment. Although expensive, the advent of short-acting, rapidly cleared IV drugs such as propofol provides veterinarians with the option of maintaining general anesthesia using continuous infusions. Two intravenous infusion doses of propofol (0.2 mg/kg per minute and 0.4 mg/kg per minute) used for anesthetic maintenance in llamas have been assessed after a 2 mg/kg induction dose (Duke et al., 1997). The infusions were maintained for 60 minutes, during which time llamas receiving the higher dose appeared adequately anesthetized and generally unresponsive to external stimuli, whereas llamas receiving the lower dose were noise sensitive and made weak attempts to raise their head. Animals stood an average of 13 to 22 minutes following termination of the low- and high-dose infusion, respectively, and showed little to no ataxia.

During anesthetic maintenance with both infusions of propofol the heart rate was increased (to approximately 90 bpm) over pre-drug values (of approximately 55 bpm). Mean carotid arterial pressure was similar to pre-drug values and ranged from an average of 103 to 147 mmHg during drug-induced recumbency. The PaCO₂ increased and PaO₂ decreased in recumbent animals, but were felt to be within a clinically acceptable range. However, three llamas did become dyspneic and required placement of a nasopharyngeal tube to ensure a patent airway.

Muscle Relaxation during General Anesthesia When muscle relaxation provided by the anesthetic agents alone is not adequate (e.g., intraocular surgery, reduction/repair of a displaced long bone fracture), drugs that block the neuromuscular junction (peripherally acting muscle relaxants) are used as adjuncts during general anesthesia. The efficacy of atracurium, administered via intermittent IV bolus (0.15 mg/kg initial dose, followed by 0.08 mg/kg) or IV infusion (0.15 mg/kg initial dose, followed by 0.4 mg/kg per hour) has been evaluated in halothane anesthetized, mechanically ventilated llamas (Hildebrand et al., 1993). Another report suggests that both succinylcholine and gallamine may be used successfully to supplement relaxation during general anesthesia in camels (Held et al., 1982). When using these agents it is essential be aware that they provide no analgesic or sedative properties and that ventilation will be significantly depressed.

ANESTHETIC RECOVERY

Although the occasional patient may have a violent recovery, in general camelids recover well from anesthesia. When possible it is ideal to place the camelid in a sternal posture with the head elevated. This allows both for eructation and helps minimize any nasal edema. Oxygen insufflation during this period is also beneficial. If the patient is orotracheally intubated, the

endotracheal tube should be protected so it does not get lacerated by the molars. In the alpaca and llama this is relatively easy to do with a partially used 2-inch roll of tape, which can be placed over the tube in the mouth with a tab hanging out. It is important not to remove the endotracheal tube until one is sure that the patient can control its airway. Camelids frequently show early arousal and chew their tube and raise their head briefly and then seemingly "fall asleep" again. Therefore, removal of the tube in this early period can result in airway obstruction. Often this is silent and only evident when observing the chest move inward (as opposed to outward) during inspiration. Intervention is critical and may be as simple as extending the head and trying to get the patient to swallow and providing oxygen; in extreme cases, re-intubation is necessary.

ANALGESIC TECHNIQUES

Although efficacy of local and regional anesthetic techniques is reported in camelids (Grubb et al., 1993; Barrington et al., 1993), there is very little published regarding benefits or side effects of systemically administered analgesics in these animals. Hence, much of the use is based on personal preference and extrapolation from other species. Evaluation is further confounded by difficulty in assessing clinical signs of and consequently resolution of pain. Although no animal should suffer because of pain, one should continue to obtain evidence for the efficacy of analgesic drugs to ensure appropriate therapy for the patient.

Non-steroidal anti-inflammatory drugs and opioids have been used and studied to a limited extent in South American Camelids (llamas). The pharmacokinetics of ketoprofen, phenylbutazone, and flunixin meglumine are described in llamas (Navarre et al., 2001a,b,c). However, as authors state, the determination of serum or plasma concentrations associated with analgesia are only extrapolated from other species; serum concentrations between 0.4 and 0.6 µg/ml of ketoprofen are considered effective in humans and a target of 5 to 15 µg/ml is suggested for phenylbutazone in horses. As plasma or serum concentrations may not truly represent therapeutic effects at the site of the lesion within the tissue, relating kinetic data to clinical efficacy is further confounded. However, these drugs continue to be used in camelids with apparent clinical success.

Use of the opioids in the clinical environment is perhaps more controversial. Although potent opioids have been used to provide immobilization, information on the use of these drugs as analgesics is limited. There is one report suggesting that use of intramuscular butorphanol (0.1 mg/kg) is of some benefit in animals experiencing somatic pain; the short half-life following intravenous butorphanol was thought to limit its clinical usefulness (Carroll et al., 2001). Mixed results were described by authors assessing analgesia produced by

morphine in healthy llamas. A dose of 0.25 mg/kg IV produced the most consistent increase in tolerance to a cutaneous electrical stimulus in this report (Uhrig et al., in press). Although studies such as these may not represent the true clinical condition, the variability in response when compared to the effects of these drugs in studies conducted in other species (e.g., dog) suggest the need for further evaluation.

MONITORING DURING ANESTHETIC-INDUCED RECUMBENCY

Monitoring anesthetic depth in camelids can be challenging because they maintain ocular reflexes at seemingly all planes of anesthesia. In addition to a brisk palpebral reflex, the globe also tends to rotate periodically during anesthesia; this is quite disconcerting to the inexperienced individual, but seems to bear little correlation with movement in response to a noxious stimulus. In the absences spontaneous eye movement, eyelid aperture (or the distance between eyelids) has been correlated and widens with increasing inhalant anesthetic depth in llamas (Mama et al., 2001). Jaw tone is another useful method for monitoring anesthetic depth in the smaller camelids. Assessment of preputial and rectal tone, drooping of the lower lip, relaxation of neck, abdominal, and tail musculature have been advocated by some as another means to assess depth of anesthesia and muscle relaxation (Alsobayil, 1999).

Guidelines for monitoring physiological responses during drug induced recumbency are much the same as for any other species. The degree of monitoring should be appropriate for the patient's health status and with regard to the procedure; monitoring a young animal undergoing a castration differ significantly from a patient needing abdominal exploratory surgery.

Monitoring for short-term chemical restraint in a field situation may include auscultation of the heart and lungs, palpation of the pulse, and evaluation of mucous membrane color and refill time. Changes in muscle tone or gross movement are commonly used to assess anesthetic depth. For longer procedures or those in which the animal may be at more risk, non-invasive battery powered monitors such as a pulse oximeter and Doppler or oscillometric blood pressure monitor may easily be placed. A rectal thermometer is used to monitor body temperature if deemed necessary. Although it is recommended that record notations be made at 5-minute intervals, it is ideal to observe the patient continuously.

In a referral hospital setting, monitoring is generally more extensive as patients are often significantly compromised. Typically in addition to pulse palpation and observation of mucous membranes, the cardiovascular system is evaluated using an electrocardiogram (ECG) to assess heart rate and rhythm and an arterial catheter is placed for direct (invasive) blood pressure monitoring. ECG leads function best when clips are placed in areas

with less fiber (axilla and flank or upper lip/base of the ear). Depending on the procedure leads should be placed on either side of the heart or cranial and caudal to the heart. Arterial catheters (20 or 22 gauge 3–5 cm) are commonly placed in the auricular or medial saphenous artery, but the carpal, cranial tibial or middle coccygeal artery may also be used in camelids. Heart rate ranges from 60 to 120 bpm in llamas and alpacas during inhalation anesthesia but may be significantly lower if α_2 -agonists are used. In camels, heart rate is more typically 40 to 50 bpm, but bradycardia and 2nd degree AV block may be observed with use of α_2 -agonists (White et al., 1987). Blood pressure in llamas and alpacas seems to be quite labile and may vary from a mean pressure of 50 to 60 to 100 mmHg for seemingly no apparent reason. Despite this studies have shown that there is a trend and blood pressure decreases with increasing inhalation anesthetic depth as has been shown for other species (Mama et al., 2001).

A thermistor probe is placed nasally or rectally for evaluation of body temperature and either a pulse oximeter (SpO₂) and capnograph or arterial blood gases (PaCO₂, PaO₂) are used to evaluate pulmonary function. Values are similar to those observed in other domestic species or in the range of 95% to 100% for SpO₂ and 40 to 50 mmHg for end-tidal and PaCO₂. PaO₂ values are influenced by the inspired oxygen and may range from 80 to 100 mmHg at sea level for a patient breathing room air to 500 mmHg for a patient breathing 100% oxygen. Keep in mind that altitude significantly decreases these values.

For critically ill patients, glucose, electrolyte, and acid-base monitoring and measurement of PCV and TP can add useful information. Note that unlike most other species apparently healthy llamas and alpacas frequently have a packed cell volume (PCV) ranging upward from the mid-20s.

Monitoring abdominal distention and for the presence (and volume) or absence of regurgitation, and for degree of nasal edema during drug induced recumbency are also important as they may indicate the need for intervention to ensure a favorable outcome.

SUPPORT DURING ANESTHETIC-INDUCED RECUMBENCY

As with monitoring, supportive care should also be related to patient's needs with some exceptions. For example, the eye should always be protected and lubricated in camelids as they tend to protrude from the head and are easily traumatized. Attention should always be given to patient positioning so as not to cause neural or muscle damage; lower forelimb pulled forward in lateral recumbency and upper limbs supported in a natural position (not hanging). In dorsal recumbency, the limbs should be flexed. For longer procedures or larger

patients padding becomes increasingly important. Air or foam mattresses and water beds have all been used successfully.

In cool environments or in young and small patients external heat should be provided, whereas active cooling may be necessary in warm environments. Circulating air or water blankets or radiant heat lamps may be used for warmth, whereas providing shade or using a fan or simply hosing the patient with water help keep the patient cool.

A balanced electrolyte solution should be administered intravenously to patients undergoing inhalation anesthesia or those in whom recumbency is expected to last greater than 1 hour. An administration rate of 5 ml/kg per hour is suggested for most patients. Dehydrated patients should receive a fluid volume appropriate for the perceived level (e.g., 5% of a 100-kg animal is equivalent to 5 L). If heart rate or blood pressure values fall out of the normal range, additional intervention may be necessary. This may include anticholinergics such as atropine and inotropes/vasopressors such as ephedrine, dobutamine, or phenylephrine.

In critically ill patients, electrolytes may need to be adjusted and acid-base balance corrected. In very young patients, glucose supplementation may be necessary. Methods for calculating and adjusting these values are available.

Although oxygen is routinely used in patients during inhalation anesthesia, this is less common when using injectable techniques. Because llamas and alpacas have been shown to become hypoxic during injectable anesthetics, oxygen supplementation is highly recommended especially for patients at altitude. Camels are also prone to hypoxemia owing to their body mass and oxygen supplementation should always be considered during recumbency. Availability of lightweight aluminum tanks and flow meters has made this easier to achieve in field conditions. The flow meter is connected to a small flexible hose placed in the ventromedial nasal meatus up to the medial canthus of the eye. An Ambu bag should be available in case of a need to ventilate a patient in the field. For a patient connected to a breathing circuit, manual or mechanical ventilation is easily accomplished.

Although uncommon in llamas and alpacas, recumbent camels may bloat and placement of a "bloat" tube may be necessary to help relieve this and minimize the influence on venous return and pulmonary function. Because these animals are obligate nasal breathers, nasal edema can be problematic following extubation. When possible, the head should be positioned to allow drainage of regurgitant fluid while still minimizing edema. Alternatively vasoconstrictors such as phenylephrine may be diluted and gently placed in the nasal passages prior to extubation. If food material is observed from the nose gentle lavage (after ensuring the endotracheal tube cuff is sealed) is recommended.

SUMMARY

Chances of a favorable outcome are increased with an understanding of basic physiological differences between camelids and other species, and selection of appropriate drug, monitoring, and supportive techniques.

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Giraffidae

Scott B. Citino and Mitchell Bush

TAXONOMY AND BIOLOGY

Giraffids were once very diverse and widespread throughout Africa, Asia, and Europe. Presently, only two genera with one species per genera are extant within the family Giraffidae, the giraffe, Giraffa camelopardalis and the okapi, *Okapia johnstoni*. Nine subspecies of giraffe have been described based on body size, color, coat pattern, and geographic distribution (Dagg, 1976; Nowak, 1983). Shared characteristics of giraffids include long legs with forelegs longer than rear legs; elongated necks; large eyes and ears; long, dark, prehensile tongues; lack of a gallbladder in most animals; thick skin with coat patterns that provide camouflage; and the presence of skin-covered ossicones that arise over the parietal bones in giraffe and the frontal bones in okapi (Dagg, 1976; Nowak, 1983; Bush, 2003). Giraffids are browsing ruminants that are highly selective feeders. Their stature allows them to exploit feeding niches unavailable to other terrestrial herbivores. Giraffe dwell primarily in Acacia, Commiphora, and Terminalia dominated savannahs and semi-arid, open woodlands, whereas okapi live in the mid-elevation, equatorial hardwood forests of northeast Democratic Republic of the Congo (Dagg, 1976; Nowak, 1983). Okapi live relatively secretive, solitary lives, whereas giraffe are more social, living in loosely organized female herds and sub-adult male bachelor groupings with solitary adult males.

ANATOMY AND PHYSIOLOGY RELATED TO ANESTHESIA

The art and science of giraffe anesthesia remains a challenge because of their unique anatomy and physiology, which presents inherent risks during chemical restraint, and consequently can result in unacceptable morbidity or mortality. Their large size and cumbersome shape limits physical control during critical times of induction and recovery, and limits manipulation once the giraffe is down. Adult giraffes range from 4.5 to 5.5 meters tall

and can weigh from 500 to 1950 kg, with males being larger (Dagg, 1976; Nowak, 1983; Bush, 2003). Even weighing giraffe during anesthetic procedures can be difficult because of their size and shape. Formulas have been published to estimate weight from body measurements (Hall-Martin, 1977). Adult okapi range in weight from 240 to 300 kg and have shoulder heights of 1.5 to 1.8 meters with females being larger (Nowak, 1983; Citino, 2006). Giraffes have a characteristic long neck, which if not controlled acts as a lever arm during inductions and recoveries, creating a danger to the giraffe and/or the support staff. Mal-positioning of the neck can lead to airway obstruction and/or cramping or focal myopathies of neck muscles, which can produce fatalities (Bush, 2002; Citino, 2006). The giraffe's long neck also presents unique problems in regard to regulation of systemic arterial blood pressure, maintenance of cerebral circulation, and generation of respiratory dead space (Langman, 1973; Warren, 1974; Hugh-Jones, 1978; Hargens, 1987, 1988; Bush, 1993, 2002, 2003; Mitchell, 1993; Pedley, 1996). To maintain cerebral circulation, giraffe maintain the highest mean arterial pressure at the level of the heart of any animal thus far studied (approximately 200 mmHg) (Hargens, 1987, 1988). In dependent areas such as the legs and feet, the mean arterial pressure may exceed 400 mmHg (Hargens, 1987, 1988). To prevent edema and pooling of fluids in dependent areas, giraffe have capillaries highly impermeable to plasma proteins, precapillary sphincters, and pronounced arterial and arteriolar wall hypertrophy, a prominent lymphatic system, one-way valves in lymphatics and veins, and tight skin and fascial layers that provide a functional "antigravity suit" and pumping mechanism during movement (Hargens, 1987, 1988). Because of the giraffe's unique cardiovascular physiology, the giraffe heart may be more prone to injury from oxygen debt during periods of hypoxemia (Linton, 1999). Giraffe are speculated to have a large respiratory dead space generated by their long trachea, which appears to be compensated for by a smaller than expected tracheal diameter, slow deep

respirations, and a large tidal volume (Hugh-Jones, 1978; Langman, 1982; Bush, 2003). The long legs of giraffe make them prone to stumbling and splaying during induction and recovery, which can lead to fractures, luxations, muscle and ligament tears, and/or nerve damage. Recumbent giraffe require good footing and sufficient room to be able to rock forward with their long neck to get their long legs underneath them to stand. Giraffe and okapi have elongated skulls (elongated diastema) with narrow inter-dental spaces that can make endotracheal intubation challenging, and the posterior position of the larynx impedes drainage of pharyngeal fluids and enhances the potential for aspiration (Dagg, 1976; Nowak, 1983; Bush, 2002). Giraffe and okapi have a tendency to regurgitate while under the influence of certain chemical restraint agents, which can lead to morbidity and mortality from aspiration pneumonia (Bush, 1993, 2002, 2003). The thick skin of giraffids requires the use of long, robust needles to assure good intramuscular injections. Giraffe can alter their body temperature to minimize water loss and help with heat regulation (Langman, 1982; Bush, 2003). Besides having a tendency toward hyperthermia from overexertion during field captures, giraffe are reported to sometime suffer from a malignant hyperthermia-like syndrome during anesthesia (Citino, 1984). Conversely, if ambient temperatures are low, giraffe and okapi tend to lose body temperature rapidly during anesthesia and can become hypothermic (Citino, 2006).

The most commonly used vascular access site in giraffids is the jugular vein. Because of thick cervical skin, the jugular vein may not always be visible but usually can be palpated and is generally more accessible closer to the head. Auricular and facial veins are also very accessible during anesthetic procedures. Through-the-needle catheters are more effective for jugular catheterization in these species. If over-the-needle catheters are used for jugular catheterization, a stab incision or partial cutdown is generally required. The auricular artery on the dorsal ridge of the ear is most often used for arterial blood collection and for arterial catheterization for invasive blood pressure measurements (Figure 52.1). Pulse oximetry transmission sensor placement is generally most effective across a scraped ear or across vulvar, mammary, prepucial, or scrotal skin. Tail cuffs appear to work best for non-invasive blood pressure measurements. Lead placement for electrocardiography is best accomplished with needles placed through the thick skin of giraffids.

ANALGESIA

The most commonly used drugs for analgesia in giraffids are non-steroidal anti-inflammatory drugs (NSAIDs) (Teare, 2000). Flunixin meglumine (intravenously [IV], intramuscularly [IM], or by mouth [PO], 1.0–2.0 mg/kg SID), phenylbutazone (PO, 1.0-3.0 mg/kg SID to BID),



Figure 52.1. Collecting a blood sample from the auricular artery for blood gas analysis.

and ketoprofen (IV or IM, 0.5 to 2.0 mg/kg SID) have been used most often (Teare, 2000; Citino, 2006). Other NSAIDs used in giraffids include etodolac (PO, 2.5–5.0 mg/kg, SID to BID), carprofen (PO, 2.0 mg/kg, SID to BID), and meloxicam (PO, 0.10 mg/kg, SID) (Citino, 2006). Low doses of butorphanol may also be effective for some types of pain.

PHYSICAL AND MECHANICAL RESTRAINT

Only very young giraffe and okapi calves can be safely restrained manually. Mattresses or flexible padding can be wrapped around older calves, or they can be pushed into a padded corner with push boards to safely restrain them for minor procedures.

Mechanical restraint of giraffes is appropriate for minimally invasive procedures such as blood sampling, tuberculin testing, rectal examinations, and minor hoof trimming, but giraffes can present dangers to handlers and themselves during such procedures. Giraffes have powerful kicks; can strike outward with their forelegs; and can swing and bash with their neck and head. If the footing is slippery, they can fall and injure themselves or ground support staff. Giraffe restraint devices vary from crates and walk-through chutes to small stalls or hallways with moveable walls to innovative mechanical or hydraulic squeeze chutes (Calle, 1988). All restraint devices should be designed to allow easy removal of a giraffe that goes down in the device. Successful mechanical restraint of giraffe is dependent on facility design, training and conditioning of the giraffe, plus a welltrained staff. A well-designed chute, with a side that opens, can also be a valuable giraffe anesthesia induction device that allows close confinement, head control, and controlled progression to sternal recumbency. Mechanical restraint has been infrequently used on

okapi; however, okapi have been conditioned to a special crate for venipuncture. Okapi are excellent kickers and the head and ossicones of males are formidable weapons.

For more extensive or invasive procedures on standing giraffe such as hoof trims, obstetrics, minor surgeries, percutaneous biopsies, etc., chemically assisted mechanical restraint can be used sometimes. This generally involves the use of an α_2 -adrenergic agonist alone or α_2 -adrenergic agonist-azaperone combination given just prior to placing a giraffe into a mechanical restraint device. Xylazine (0.10-0.2 mg/kg IM), detomidine (15–40 μg/kg IM), xylazine-azaperone (0.10–0.12 mg/kg IM; 0.20–0.50 mg/kg IM), and detomidine-azaperone $(15-30 \mu g/kg IM; 0.25-0.35 mg/kg IM)$ have been most commonly used for this purpose (Bush, 2002, 2003; Citino, 2006). To increase sedation and analgesia, low doses of butorphanol (10–20 mg IV total) can be given to adult giraffe (Citino, 2006). Giraffe given these drugs in a restraint device can potentially become ataxic and go down, so handlers should always be prepared for this. Xylazine and detomidine can be partially reversed with yohimbine (0.10–0.20 mg/kg IV or IM) or atipamezole (0.10–0.20 mg/kg IV or IM), and butorphanol can be reversed with naltrexone (2.0 mg naltrexone/mg of butorphanol IV or IM) (Bush, 2002, 2003; Citino, 2006).

SEDATION AND TRANQUILIZATION

Standing sedation for hands-on procedures is rarely attempted in older giraffe outside of a restraint device because of the potential danger these animals pose to handlers. α_2 -Adrenergic agonists at the suggested doses above can be used for safer manipulations in enclosures and chutes, for getting reluctant dams to allow calves to nurse, and to calm animals in stressful or dangerous situations (Fischer, 1997; Bush, 2002, 2003; Citino, 2006). It should always be remembered that giraffe under α_2 adrenergic agonist sedation can still kick, strike, and rapidly arouse from sedation and become very dangerous. Azaperone has also been used at 0.20 to 0.50 mg/kg IM as a short-acting, calming and stress-reducing agent in giraffe (Citino, 2006). Intermediate and long-acting neuroleptics that have been used in adult giraffe include haloperidol (Male, 20–30 mg IM; Female, 15–20 mg IM), zuclopenthixol acetate (100-300 mg IM), and perphenazine enanthate (100-250 mg IM) (Ebedes, 1995; Citino, 2006). Haloperidol has its onset in about 15 minutes and its effects last for 15 to 24 hours; zuclopenthixol acetate has its onset in 1 to 6 hours and its effects last about 3 days; and perphenazine enanthate has its onset in about 2 to 3 days and its effects last for 7 to 10 days (Ebedes, 1995). Giraffe appear sensitive to these neuroleptic agents, and untoward effects such as anorexia and extrapyramidal effects are common (Citino, 2006). Because of a significant potential for disorientation, unsteadiness on their feet, and collapse in their transport container, the use of sedatives and/or neuroleptic agents in giraffe during transport is considered risky and should only be done with great care.

Standing restraint in adult okapi for minor procedures such as venipuncture, physical examination, obstetrics, radiography, catheter placement, etc. has been accomplished with xylazine given at 125 to 300 mg IM (0.50-1.20 mg/kg IM) (Citino, 1996, 2006; Raphael, 1999; Teare, 2000). Xylazine can be partially reversed with yohimbine (0.10-0.20 mg/kg IV or IM) or tolazoline (0.50 mg/kg IV or IM) (Citino, 1996, 2006; Raphael, 1999). More complete reversal of xylazine has been achieved with the experimental α_2 -adrenergic antagonist RX821002 (5.0 mg total dose IV) or combinations of yohimbine or tolazoline and atipamizole (30–100 μg/kg IV or IM) (Citino, 1996, 2006; Raphael, 1999; Teare, 2000). For okapi that appear resistant to xylazine alone, the addition of azaperone (0.20–0.40 mg/kg IM) may improve the standing restraint (Citino, 2006). Good standing restraint for venipuncture, catheter placement, vaginal insemination, etc. has also been achieved with xylazine (0.40-0.80 mg/kg IM) or detomidine (40-100 µg/kg IM) with butorphanol (80–200 μg/kg IM) (Teare, 2000; Citino, 2006). Butorphanol has been reversed with naltrexone (1.0 mg/mg butorphanol IV or IM) (Citino, 2006). Azaperone (0.20-0.50 mg/kg IM) and haloperidol $(80-100 \mu\text{g/kg})$ IM) have been used to tranquilize flighty animals when moved or manipulated in enclosures (Citino, 1996, 2006; Raphael, 1999). Haloperidol (0.90–1.50 mg/kg) has also produced mild calming effects when given orally to okapi (Citino, 2006). The intermediate-acting neuroleptic zuclopenthixol acetate (0.40–1.0 mg/kg IM) has been used to reduce stress and calm animals during transport (Raphael, 1999; Citino, 2006). A combination of zuclopenthixol acetate (100 mg IM 15 hours before move) and haloperidol (10-20 mg IM to facilitate crating) was used to load and transport two okapi that were not crate trained (Redrobe, 2003).

ENDOTRACHEAL INTUBATION

A 40- to 60-cm laryngoscope blade is required to visualize the glottis in adult giraffe, whereas a 30- to 40-cm laryngoscope blade suffices in okapi (Citino, 2006). Adult giraffe generally take endotracheal tubes with internal diameters of 24 to 30 mm, whereas adult okapi generally take tubes of 20 to 26 mm (Citino, 2006). Giraffids are best intubated using the Bush technique: visualizing the glottis with a laryngoscope, passing a tracheal exchange catheter through the glottis, threading the exchange catheter through the Murphy's eye of the endotracheal tube, and passing the tube through the glottis using the exchange catheter as a guide (Bush, 1996). In large giraffe, the glottis can be digitally palpated and an endotracheal tube manually placed. Giraffids can also be intubated by passing a fiberoptic

endoscope through the endotracheal tube, visually passing the endoscope into the trachea, and then using the endoscope as a stylet to place the tube. The authors recommend using a cuffed endotracheal tube to intubate giraffe that will be anesthetized for longer than 15 minutes. Oxygen can then be supplied by insufflation or jet ventilation and respiratory support can be given with a one- or two-demand valve system or field ventilator.

ANESTHESIA OF GIRAFFE

Even with the development of newer and safer drugs and improved physiological monitoring equipment, giraffe anesthesia remains a major challenge because of their unique anatomy and physiology. Despite the frequent need to capture and relocate this species in situ, giraffe are still considered a high-risk species to chemical capture because of their large size and unique physiology and handling problems. Because of their awkward shape, weight estimation and dosage calculation are difficult, especially in the field. All of these special characteristics predispose them to life-threatening, anesthesiarelated complications, including: (1) vomiting/passive regurgitation leading to fatal inhalation pneumonia; (2) respiratory depression and hypoventilation with resulting hypoxemia and hypercarbia; (3) tachycardia, hypertension, bradycardia, hypotension, or other significant cardiac emergencies; (4) self-induced trauma during induction and/or following reversal; and (5) hyperthermia and/or capture myopathy secondary to prolonged and stormy induction and incomplete anesthesia reversal (Citino, 1984; Bush, 1993, 2002, 2003). The historical high morbidity and mortality encountered during giraffe anesthesia, in both captive and freeranging settings, leads to a hesitancy to anesthetize them.

Historical verbal and published reports describe the use of several drugs and drug combinations for giraffe anesthesia. Drugs used alone or in combination have included succinylcholine, gallamine, hyoscine, atropine, hyaluronidase, glycerol guaiacolate, acepromazine, azaperone, xylazine, detomidine, medetomidine, ketamine, telazol, barbiturates, butorphanol, fentanyl, etorphine, carfentanil, and thiafentanil (A3080) (Hirst, 1966; Williamson, 1968; Langman, 1973; York, 1973, 1975; Rapley, 1975; Bush, 1976, 1987, 1993, 1997, 2001, 2002, 2003; Gardner, 1986; Weisner, 1989; Vahala, 1990; Geiser, 1992; Morkel, 1992, 1993; Fischer, 1997; Vogelnest, 1997; Lamberski, 2004; Citino, 2006; Raath, 2006).

Many of the problems associated with anesthesia can be minimized in captive giraffe with careful preplanning and forethought. An experienced staff to assist with the critical induction and recovery phases of anesthesia and for monitoring the patient is essential. Fasting of animals is probably over-emphasized and need only occur for a maximum of 24 hours, with concentrate being the primary foodstuff to withhold.

Animals should be prevented from drinking large quantities of water just prior to anesthesia by withholding water for 6 to 24 hours depending on climatic conditions. The site and method of induction are also critical for success. The use of a well-designed chute for giraffe induction can greatly reduce risk and allow a staged and controlled induction to occur (Calle, 1988; Bush, 2003; Citino, 2006). The chute must be designed so forward pressing or falling will not compromise respiration, with no potential foot, leg, or neck traps, and with a complete side that swings open to allow easy removal and positioning of the giraffe. If a suitable chute is not available a confined space with smooth solid walls, lack of trip and fall hazards, and a catwalk for access to the animal's head during the procedure can be used. If a catwalk is absent around the induction area and a halter can be placed before or during induction, a ceiling pulley and rope apparatus can be used to suspend the animal's head and neck during induction to reduce falling injuries and prevent head slamming. If the giraffe must be induced in a larger area without head control, all tripping and falling hazards should be removed or minimized and methods for keeping the giraffe away from dangerous pressing points and head and neck traps should be determined. No matter where giraffe anesthesia is accomplished, good footing is mandatory to prevent slipping and splaying. Also, adequate staff and/or equipment should be present to move an animal quickly, if necessary. Since complications can occur rapidly in anesthetized giraffe, close physiological monitoring is essential for patient safety and should include both the usual visual and tactile monitoring as well as electronic monitoring (i.e., temperature, pulse oximetry, capnography, invasive and non-invasive blood pressure, electrocardiography, and arterial blood gas and pH measurements). Perhaps the hardest thing to do is back off from a procedure. Many procedures involving giraffe require extensive coordination to make sure that people, facilities, and equipment are ready. Unless conducting an emergency procedure, if something is not going right or if there is a factor that can be changed to enhance the success of the procedure, it should be stopped and rescheduled. Even with the most careful planning and preparation, procedural complications can still occur in captive situations but are amplified in free-ranging giraffes because there is minimal control of the situation.

There are standardized procedures for handling an anesthetized giraffe in lateral recumbency, which include supporting the neck with a board or ladder so the head is maintained above the rumen with the nose pointed down to facilitate drainage of fluids. The neck should be kept straight without kinks or angulations. The angle of the neck is altered every 10 to 15 minutes and the neck can be massaged to minimize muscle spasms, which can be life threatening in the post recovery period. Padding should be placed under the giraffe, particularly under

the shoulder and radius to prevent pressure trauma to the radial nerve. Oxygen should be supplied by either nasal insufflation or endotracheal tube (Figures 52.2 to 52.4).

Recovery is a very critical time in a giraffe anesthetic procedure. Good footing is essential during recovery, as is adequate space for the giraffe to rock forward and gain the momentum to stand. If the giraffe does not regain its feet within 45 minutes of administration of the antagonist, the prognosis is poor for the animal's recovery. The route of administration of the antagonist can greatly influence recovery. Intramuscular administration of the antagonists generally provides the slow, controlled recovery that is generally preferred (Bush, 2002, 2003; Lamberski, 2004; Citino, 2006). Many times with IV administration of antagonists, giraffe become excited, try to stand before they are ready, and fall, potentially injuring themselves.

The most widely used anesthetic regimens for giraffe have involved use of opioids alone or in combination with sedatives (e.g., xylazine), tranquilizers (e.g., azaparone), and/or absorption accelerants (e.g., hyaluronidase) and, most recently, the potent specific α_2 -adrenergic agonist medetomidine with ketamine (Hirst, 1966; Williamson, 1968; Langman, 1973; York, 1973, 1975; Rapley, 1975; Bush, 1976, 1987, 1993, 1997, 2001, 2002, 2003; Weisner, 1989; Vahala, 1990; Geiser, 1992; Morkel, 1992, 1993; Volgenest, 1997; Lamberski, 2004).

A staged protocol using etorphine and xylazine has been used commonly in the past for anesthesia of captive giraffe (Bush, 1976, 1993, 2002, 2003). This approach tends to cause less respiratory depression because etorphine doses can be titrated to the needs of the individual animal and situation. This protocol is



Figure 52.2. Subadult free-ranging giraffe immobilized with thiafentanil-medetomidine-ketamine at Kariega Reserve, Eastern Cape, South Africa. Notice head and neck elevated on ladder, physiological monitors in place, and blindfold and halter in place. Animal is safe for large number of people to be around it.

ideally carried out in a chute or confined area in which head control can be maintained. Initially, giraffe are given xylazine (70–100 mg/adult or 30–40 mg/yearling IM). Atropine (7.0–8.0 mg/adult or 2.0–3.0 mg/yearling IM) can be given simultaneously to prevent xylazineinduced bradycardia. Five to ten minutes after xylazine administration, signs of sedation occur (i.e., stargazing, ataxia, and tongue protrusion with slight salivation). About 15 to 20 minutes after the xylazine, a narcotizing dose of etorphine (1.5-2.5 mg/adult or 0.5-1.25/yearling IM) is administered. This dose may induce recumbency within 15 to 20 minutes. Ideally, a head halter, placed when the animal is narcotized, is used to help control the head and assist the animal to the ground, without tumbling over backward. If the giraffe does not become recumbent after etorphine administration, it can be supplemented with etorphine (0.5–1.0 mg IM or IV),



Figure 52.3. Subadult free-ranging giraffe immobilized in Kruger National Park, South Africa. Notice head and neck elevated with ladder and blindfold.



Figure 52.4. Subadult free-ranging giraffe immobilized in Kruger National Park, South Africa with thiafentanil-medetomidine-ketamine. Notice physiologic monitors: Pulse oximetry with transducer on scraped ear, capnography.

5% guaifenesin solution IV to effect, or ketamine (100–400 mg IV), or can be physically cast. For reversal of etorphine, naltrexone (50–100 mg/mg etorphine, 1/2 IV 1/2 IM or all IM) is given and for xylazine, yohimbine (0.10–0.20 mg/kg IV or IM) or atipamezole (50–100 mg total 1/4 IV 3/4 IM or all IM) is given. It is possible to substitute carfentanil (1.2–2.1 mg/adult or 0.30–0.90/yearling IM) for etorphine in this protocol (Citino, 2006).

Current methods for capture of free-ranging giraffe use high doses of opioids alone for rapid induction and no lingering drug effects during transport. Etorphine (8.0–15.0 mg/adult), thiafentanil (8.0–16.0 mg/adult), or a combination of etorphine (4.0 mg/adult) and thiafentanil (8.0-16.0 mg/adult) with or without hyaluronidase are most commonly used (Morkel, 1992, 1993; Citino, 2006). Giraffe become narcotized rapidly, but many must be cast with ropes. Once down, muscle relaxation is poor, animals require significant restraint, and most must be fully or partially reversed with diprenorphine or naltrexone to prevent severe hypoxemia while hoods, ear plugs, and ropes are applied. This anesthetic technique greatly limits what can safely be done to a giraffe while it is recumbent. Once reversed, giraffe are very active and can be a danger to themselves and the ground crew during loading for transport (Figure 52.5). This method is for capture only and requires a well-trained and experienced capture team to safely cast, restrain, and load giraffe for transport. Most recently, a combination of thiafentanil and butorphanol has been used for capture of free-ranging giraffe, with less respiratory depression, probably owing to the partial µ opioid receptor antagonist effect of butorphanol (Raath, 2006).



Figure 52.5. Free-ranging giraffe in Kruger National Park, South Africa shortly after reversal of thiafentanil anesthesia. Notice blindfold, halter, lead rope, body ropes, and capture crew in place for loading giraffe into field chariot for transport out of veldt. Notice potential for hind limb splaying despite good footing in the field and the requirement for the giraffe to rock forward to stand.

A non-narcotic alternative for giraffe chemical restraint is the combination of medetomidine and ketamine. This combination has been used successfully in captive and free-living giraffes with dosages correlated to the giraffe's shoulder height. In "calm" animals (150 μ g medetomidine + 3.0 mg ketamine/cm of shoulder height) provided a rapid and relatively uneventful induction (Bush, 1997, 2001, 2003). Larger giraffes experienced a less desirable immobilization, which may indicate the dosage correlation to shoulder height may



Figure 52.6. Free-ranging giraffe starting to stand after reversal of thiafentanil-medetomidine-ketamine anesthesia. Notice blindfold, earplugs, halter, and ropes in place for loading giraffe into the chariot in the background. Notice potential for rear limb splaying despite good footing in the field.



Figure 52.7. Free-ranging giraffe at Kariega Reserve, Eastern Cape, South Africa after reversal of thiafentanil-medetomidine-ketamine anesthesia. Notice ropes, straps, and capture crew in position to load giraffe into chariot for transport out of veldt.

not be appropriate in larger animals. Another retrospective study in 30 captive giraffe recommends doses of medetomidine (subadult, 18-20 mg; adult female, 40-50 mg; adult male, 50-70 mg) and ketamine (subadult, 300-500 mg; adult female, 800-900 mg; adult male, 1,000-1,200 mg) (Lamberski, 2004). A nice characteristic of this combination is smooth inductions with animals usually sitting down in sternal recumbency before rolling over laterally. With medetomidineketamine, an inverse relationship is observed between the level of excitement and the quality of the immobilization: the more excited the giraffe prior to and after darting, the more physical restraint is required to bring the animal to a sternal position. This combination also produces a characteristic tachypnea (50-60 breath/ minute) and inadequate analgesia for painful procedures. Administration of atipamezole (350 µg/cm of shoulder height or five times the medetomidine dose IM) results in a rapid and usually complete reversal. Re-sedation has been seen in some giraffe given medetomidine 3 to 28 hours after reversal, therefore giraffes should be monitored closely during this time, and additional atipamazole should be administered if signs of re-sedation occur (Lamberski, 2004; Citino, 2006). Re-sedation appears to occur most commonly in the Rothschild's (G.c. rothschildi) and Southern giraffe (G. c. giraffe) subspecies and less commonly in the reticulated (G. c. reticulata) subspecies (Citino, 2006). Signs of medetomidine re-sedation include decreased awareness to surroundings, dull eyes, inappetance, lowered neck, widened stance, salivation, tongue protrusion, excessive licking, ataxia, leaning against objects, and recumbency (Lamberski, 2004; Citino, 2006).

A newer drug combination, thiafentanil-medetomidine-ketamine, has safely and successfully been used for chemical restraint of captive and free-ranging giraffe (Citino, 2006). Dosing requirements are markedly different between captive (thiafentanil $5.8 \pm 1.5 \mu g/kg +$ medetomidine 12.9 \pm 5.1 μ g/kg+ ketamine 0.65 \pm 0.18 mg/kg IM), free-ranging, ground-darted (thiafentanil $6.6 \pm 1.5 \,\mu\text{g/kg} + \text{medetomidine } 15.9 \pm 3.7 \,\mu\text{g/kg} +$ ketamine 0.50 ± 0.19 mg/kg IM), and free-ranging, helicopter-darted (thiafentanil 10.0 \pm 4.0 μ g/kg + medetomidine $14.0 \pm 9.4 \,\mu\text{g/kg} + \text{ketamine } 0.39 \pm 0.20$ mg/kg IM) giraffe. The degree of excitement associated with helicopter darting appears to negate the effects of medetomidine and makes this combination less suitable for helicopter darting. In calm animals, onset of action is ultra-rapid, with most animals down in 2 to 5 minutes. Giraffe exhibit excellent muscle relaxation and are very safe to work around with this combination. Analgesia appears very good and there is a long duration of action, so it appears useful for surgical and prolonged major procedures. A marked apneustic breathing pattern is often seen and moderate to severe hypoxemia can occur, so oxygen supplementation and/or respiratory support are recommended. Anesthesia is reversed with naltrexone (30 mg/mg thiafentanil IV or IM) and atipamezole (3–5 times the medetomidine dose IV or IM). Recoveries are best when antagonists are administered IM (Figures 52.6, 52.7). As with medetomidine-ketamine, evidence of medetomidine-associated re-sedation is seen in some giraffe post-reversal requiring additional supplements of atipamezole (Citino, 2006). Re-sedation can be a potentially life-threatening problem in giraffe, especially during transport and when giraffe are not observed closely for signs of re-sedation post-recovery.

The reader is referred to the references for published methods of giraffe anesthesia and more detailed descriptions of these procedures.

OKAPI ANESTHESIA

In comparison with giraffe, far fewer inherent problems can occur during okapi anesthesia because of their more conventional size and shape. However, complications associated with anesthesia are still one of the most significant causes of adult morbidity and mortality in the international captive population (Raphael, 1999; Citino 2006). The most common anesthesia-associated problems reported in okapi are regurgitation and aspiration of rumen contents and post-anesthesia gastrointestinal stasis or ileus (Citino, 2006).

Chemical immobilization of okapi is most commonly accomplished with an opioid (carfentanil or etorphine) in combination with an α_2 -adrenergic agonist (xylazine) or tranquilizer (acetylpromazine) (Mortelmans, 1978; Citino, 1996, 2006; Raphael, 1999; Teare, 2000). Okapi should not be fasted for longer than 12 to 24 hours prior to anesthesia as hypoglycemia and electrolyte imbalances can be induced (Citino, 2006). Water can be withheld for 6 to 12 hours, depending on climatic conditions. Inductions with opioid combinations can sometimes be stormy, with okapi stumbling, crashing, exhibiting opisthotonus, falling backwards, and flailing and head-slamming once down. It is important to induce okapi in relatively small enclosures with good footing, smooth walls, and lack of trip and fall hazards. Once an okapi is well-narcotized, two to three welltrained handlers should use controlled restraint to smooth the induction and prevent injury (Figure 52.8). A padded stall with a hinged crush wall also works nicely for preventing injuries during induction. Once down, the animal is placed sternal with its head above its rumen and nose down, is blindfolded, and given oxygen by nasal insufflation (see Figure 52.9). If the okapi must be placed in lateral recumbency, adequate padding should be placed under pressure points. As with most ruminants, okapi should not be rolled onto their back unless intubated, as this can stimulate regurgitation of rumen contents. Okapi should be kept warm during anesthesia as they have a tendency to become hypothermic (Citino, 2006).



Figure 52.8. Adult okapi being anesthetized in a staged manner with xylazine-carfentanil. Animal is displaying good narcotization from second dart containing carfentanil. Head up and pressing in corner. Handlers are preparing to assist animal into recumbency.



Figure 52.9. Captive adult male okapi anesthetized with xylazine-carfentanil. Notice head elevated and nose down, blindfold, physiological monitors, and nasal insufflation with oxygen with small endotracheal tube placed in nostril, and non-invasive blood pressure with cuff placed on tail.

Over 150 successful okapi procedures without one mortality have been completed using carfentanil and xylazine in a staged technique (Citino, 1996, 2006). Xylazine (0.12 \pm 0.02 mg/kg IM, adult total dose = 30–45 mg IM) is given first and is followed in 15–20 min

with carfentanil (4.7 \pm 0.8 μ g/kg IM, adult total dose = 0.9-1.5 mg IM). This staged technique requires less opioid and produces a much smoother induction, with better muscle relaxation, than combining the opioid and xylazine together. The better the initial sedation from xylazine, the smoother the induction will be generally. Azaperone (50.0 mg average total adult dose) can be added to the xylazine to increase sedation and improve inductions in problem animals. For okapi receiving significant stimuli during anesthesia (e.g., electroejaculation), ketamine (1.0-1.5 mg/kg) can be added to the carfentanil dart to potentiate the xylazine and carfentanil. If supplements are needed to prevent struggling, improve muscle relaxation, or deepen anesthesia, xylazine (2.0-5.0 mg boluses IV), ketamine (50–200 mg boluses IV), and 5% guaifenesin solution IV drips have been used. Naltrexone (100 mg/mg carfentanil 1/2 IV 1/2 SQ) is used to reverse the carfentanil, and yohimbine (0.10-0.20 mg/kg IV), tolazoline (100 mg IV total adult dose), RX821002 (5.0 mg IV total adult dose), or atipamezole (0.125 mg/ kg IV) is used to reverse the xylazine. After reversal, two experienced handlers should stay with the okapi to prevent injury until it is standing. Re-narcotization is occasionally seen in okapi anesthetized with carfentanil, so animals should be observed closely for 24 hours and supplemented with naltrexone if necessary (Citino, 2006).

Etorphine can also be used in a staged anesthetic technique with xylazine (Citino, 1996; Raphael, 1999; Teare, 2000). As above, xylazine (40–50 mg IM total adult dose) is first given, followed in 15 to 30 minutes by etorphine (4.0–5.0 mg IM total adult dose). There appears to be a greater risk of regurgitation with etorphine versus carfentanil in okapi (Citino, 1996; Raphael, 1999; Teare, 2000). Etorphine is reversed with naltrexone (30–50 mg/mg etorphine IV) or diprenorphine (2.0 mg/mg etorphine IV).

The non-narcotic combination of medetomidine $(60\text{--}120~\mu\text{g/kg IM})$ and ketamine (1.0--3.0~mg/kg IM) can be used to induce a deep sedation in okapi adequate for most minor procedures (Citino, 1996; Raphael, 1999; Teare, 2000). Induction generally takes 15 to 20 minutes and is generally much smoother than with opioid combinations. Animals will still kick during induction so should not be approached until down and relaxed. Okapi should not be reversed for 15 to 20 minutes post-induction to reduce unsteadiness from residual ketamine. Medetomidine is reversed by atipamezole (5.0 mg/mg medetomidine IV or IM) (Tables 52.1 and 52.2).

Table 52.1. Drugs used for chemical restraint in giraffe.

Drug	Dosage	Reversal Agent/Dose	Purpose
Xylazine	0.10-0.20 mg/kg IM	Yohimbine (0.10–0.20 mg/kg IV or IM) Atipamezole (0.10–0.20 mg/kg IV or IM)	Sedation or Chemically assisted mechanical restraint
Detomidine	$15-40\mu\mathrm{g/kg}$ IM	Yohimbine (0.10–0.20 mg/kg IV or IM) Atipamezole (0.10–0.20 mg/kg IV or IM)	Sedation or Chemically assisted mechanical restraint
Azaperone	0.20-0.50 mg/kg IM	None	Tranquilization, calming, or stress reduction
Haloperidol	Adult Male: 20–30 mg IM Adult Female: 15–20 mg IM	None	Neuroleptic, untoward effects possible
Zuclopenthixol acetate	Adult:100–300 mg IM	None	Intermediate–acting neuroleptic, untoward effects possible
Perphenazine enanthate	Adult: 100–250 mg IM	None	Long-acting neuroleptic, untoward effects possible
Xylazine + azaperone Butorphanol if needed	X: 0.10–0.12 mg/kg IM A: 0.20–0.50 mg/kg IM B: 10–20 mg total IV	Same as above for xylazine B: Naltrexone 2.0 mg/mg butorphanol IV	Chemically assisted mechanical restraint
Detomidine + azaperone Butorphanol if needed	D: 15–30 μg/kg IM A: 0.25–0.35 mg/kg IM B: 10–20 mg total IV	Same as above for detomidine B: Naltrexone 2.0 mg/mg butorphanol IV	Chemically assisted mechanical restraint
Etorphine + xylazine	X: Adult: 70–100 mg IM X: Yearling: 30–40 mg IM After sedation followed by: E: Adult: 1.5–2.5 mg IM E: Yearling: 0.5–1.25 mg IM	Same as above for xylazine E: Naltrexone 50–100 mg/mg etorphine IV or IM	Staged protocol for anesthesia of captive giraffe
Carfentanil + xylazine	X: Same as for etorphine + xylazine After sedation followed by: C: Adult: 1.2–2.1 mg IM C: Yearling: 0.20–0.90 mg IM	Same as above for xylazine C: Naltrexone 100 mg/mg carfentanil IV or IM	Staged protocol for anesthesia of captive giraffe
Thiafentanil + medetomidine + ketamine	T: $5.8 \pm 1.5 \mu\text{g/kg IM}$ M: $12.9 \pm 5.1 \mu\text{g/kg IM}$ K: $0.65 \pm 0.18 \text{mg/kg IM}$	T: Naltrexone 30 mg/mg thiafentanil IV or IM M: Atipamezole 3 to 5 times the medetomidine dose IV or IM	Protocol for captive giraffe, medetomidine re–sedation can occur, good analgesia for surgery
Medetomidine + Ketamine	M: 150 µg/cm Shd Hgt K: 3.0 mg/cm Shd Hgt or M: Male: 50–70 mg IM M: Female: 40–50 mg IM M: Subadult: 18–20 mg IM K: Male: 1,000–1,200 mg IM K: Female: 800–900 mg IM K: Subadult: 300–500 mg IM	Atipamezole (350 µg/cm Shd Hgt) or 3 to 5 times the medetomidine dose IM	Protocol for captive giraffe, medetomidine re-sedation can occur, inadequate analgesia for surgery
Etorphine	Adult: 8–15 mg IM	Naltrexone 30–100 mg/mg etorphine IV or Diprenorphine 2.0 mg/mg etorphine IV	Protocol for free-ranging giraffe
Etorphine + Thiafentanil	E: Adult: 4.0 mg IM T: Adult: 8–16 mg IM	Naltrexone 30–100 mg/mg opioid IV or Diprenorphine 2.0 mg/mg opioid IV	Protocol for free-ranging giraffe
Thiafentanil	Adult: 8–16 mg IM	Naltrexone 30 mg/mg thiafentanil IV or Diprenorphine 2.0 mg/mg thiafentanil IV	Protocol for free-ranging giraffe

Table 52.2. Drugs used for chemical restraint in okapi.

Xylazine	X: 0.50–1.20 mg/kg IM X: Adult: 125–300 mg IM	Partial reversal: Yohimbine 0.10–0.20 mg/kg IV or IM or Tolazoline 0.50 mg/kg IV or IM	Standing restraint for minor procedures
and can add if needed: Azaperone	A: 0.20-0.40 mg/kg IM	Better reversal: RX821002 5.0 mg IV or Yohimbine or Tolazoline + Atipamezole 30–100 μg/kg IV or IM	
Azaperone	0.20-0.50 mg/kg IM	None	Tranquilization, calming, or stress reduction
Haloperidol	80–100 μg/kg IM 0.90–1.5 mg/kg PO	None	Neuroleptic
Zuclopenthixol acetate	0.40-1.0 mg/kg IM	None	Intermediate-acting neuroleptic
Xylazine + butorphanol	X: 0.40-0.80 mg/kg IM	Same as above for xylazine	Standing restraint for minor procedures
	B: 80 – $200\mu g/kg$ IM	B: Naltrexone 1.0 mg/mg butorphanol IV or IM	•
Detomidine + butorphanol	D: 40–100 μg/kg IM B: 80–200 μg/kg IM	D: Same as for xylazine above B: Same as above for butorphanol	Standing restraint for minor procedures
Carfentanil + xylazine	$X: 0.12 \pm 0.02 \text{mg/kg IM}$ X: Adult: 30-45 mg IM After sedation followed by:	X: Same as for xylazine above C: Naltrexone 100 mg/mg carfentanil IV SQ	Staged protocol for anesthesia of captive okapi
	C: $4.7 \pm 0.8 \mu g/kg IM$ C: Adult: $0.9-1.5 mg IM$		
Etorphine + xylazine	X: Adult: 40–50 mg IM After sedation followed by: E: Adult: 4.0–5.0 mg IM	X: Same as for xylazine above E: Naltrexone 30–50 mg/mg etorphine IV or Diprenorphine 2.0 mg/mg etorphine IV	Staged protocol for anesthesia of captive okapi, greater risk of regurgitation with etorphine
Medetomidine + ketamine	M: 60–120 μg/kg IM K: 1.0–3.0 mg/kg IM	Atipamezole 5 times the medetomidine dose IV or IM	Protocol for captive okapi

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53

Deer (Cervids)

Nigel Caulkett and Jerry C. Haigh

INTRODUCTION

A variety of deer species are distributed worldwide. It is beyond the scope of this chapter to discuss each species; therefore, the emphasis is placed on general principles with a brief discussion of current techniques in selected species.

PRE-ANESTHETIC CONSIDERATIONS

Several factors can influence the method of anesthesia and means of drug administration. It is important to plan the capture carefully, as prolonged chase times can result in capture myopathy, trauma, or hyperthermia.

Elective procedures in captive animals should be planned for the cool hours of the day. Ruminal tympany can be a complication during anesthesia. If the procedure is elective, captive deer should be fasted for 24 hours. Deer are prone to hypoxemia during anesthesia (Murray et al., 2000; Moresco et al., 2001; Read et al., 2001). Hypoxemia is exacerbated by positioning in dorsal or lateral recumbency. α_2 -Agonist drugs such as xylazine or medetomidine will also exacerbate hypoxemia (Read et al., 2001). Chronically debilitated animals and animals with severe fluid deficits or blood loss are generally not good candidates for anesthesia, and are at increased risk for complications.

MONITORING AND SUPPORTIVE CARE

Pulmonary Function

Whenever possible deer should be positioned in sternal recumbency. The head and neck should be extended to maintain a patent airway. The animal should be monitored for hypoxemia, ideally with a pulse oximeter. A multi-site sensor applied to the tongue generally provides a good signal. Normal hemoglobin saturation should be 95% to 98%; below 85% is considered hypoxemic. Severely hypoxemic animals are often tachycardic. Heart rates above 150 in mature deer may result

from a stress response owing to hypoxemia, hypercarbia, pain, or hypotension. Tachycardia, followed by severe bradycardia (heart rate less than 30) is often a sign of impending cardiac arrest. Supplemental inspired oxygen should be considered in hypoxemic animals. Oxygen can be easily delivered via nasal insufflation (Read et al., 2001). A nasal catheter should be placed and threaded as far as the medial canthus of the eye. A flow rate of 6 to 8 L/minute is generally sufficient for smaller species, such as white-tailed deer. A flow rate of 8 to 10 L/minute may be required in larger deer species, such as red deer and moose (Figure 53.1). The oxygen flow rate is adjusted to achieve an SpO₂ of 95% or more.

In order to conserve oxygen and prolong tank life, the flow should be adjusted downward to find the minimum flow that will allow maintenance of SaO_2 greater than or equal to 95%.

Intubation can be difficult in cervids. The best technique is to maintain the animal in sternal recumbency with the head and neck extended upward. Use a laryngo-scope with a long flat blade and stiffen the endotracheal tube with a stylet. The epiglottis is long and mobile in cervids. The flat blade of the laryngoscope should be carefully placed on the dorsum of the epiglottis, depressing it ventrally. The opening to the glottis can then be visualized and intubation can proceed. Animals induced with xylazine and ketamine may swallow or close the glottic opening during intubation. The depth of anesthesia may be increased, to facilitate intubation, with an additional dose of ketamine (1–2 mg/kg) or propofol (2–4 mg/kg) (Woodbury et al., 2002).

Monitoring the Cardiovascular System

Heart rate should be monitored, at minimum, every 5 minutes. The auricular artery is easily palpated in deer. If the auricular artery cannot be palpated, a femoral pulse can be used. Blood pressure can be easily measured with an oscillometric cuff placed proximal to the carpus. Hypertension (systolic pressure greater than 200 mmHg) can be encountered when medetomidine is used.



Figure 53.1. Nasal insufflation of oxygen to a moose. The oxygen flow rate is adjusted to achieve an SpO_2 of 95% or more.

Thermoregulation

Rectal temperature should be monitored every 5 to 10 minutes. Deer are prone to hyperthermia (Moresco et al., 2001; Read et al., 2001). Rectal temperatures greater than 40°C are cause for concern, and attempts should be made to cool the animal. Rectal temperature in excess of 41°C is an emergency and should be treated aggressively. It is difficult to actively cool large animals and often the best option is to antagonize the immobilizing agents and allow the animal to recover. Hyperthermia, in the face of hypoxemia, is a particularly serious complication, as hyperthermia increases metabolic oxygen demand. Hyperthermic animals should receive supplemental inspired oxygen to offset hypoxemia.

Complications

Maintenance in sternal recumbency helps prevent the development of ruminal tympany. If ruminal tympany is a problem, the animal may be rocked gently to stimulate eructation. A rumen tube can be used, but may predispose to regurgitation and aspiration. Generally, if ruminal tympany is severe, it is advisable to finish the procedure quickly and antagonize the anesthetic agents. If α_2 -agonists have been used, the administration of tolazoline, yohimbine, or atipamezole will stimulate ruminal activity and relieve ruminal tympany.

Capture myopathy is a potentially serious complication that can be very difficult to treat (Spraker, 1993). Capture myopathy can be acute. In the acute form of capture myopathy the animal's oxygen demand is far in excess of oxygen supply. Animals often present with hyperthermia, cyanosis, acidosis, tachycardia, and hypotension. The animal may die during the anesthetic or soon after. If the animal survives the acute stage it may develop subacute or chronic capture myopathy. This can have a variety of manifestations, including paraplegia, ruptured muscles, myoglobinuria, or olig-

uria (Spraker, 1993). The treatment of acute capture myopathy is directed at symptomatic treatment for shock, correcting acid-base disturbances, and maintaining normothermia and oxygenation. Treatment is extremely difficult in a field situation and is often unsuccessful. Animals with chronic capture myopathy generally need to be euthanized. It is best to prevent capture myopathy by keeping chase times to a minimum and avoiding prolonged physical restraint.

Trauma is not uncommon during capture. White-tailed deer can be very flighty and, as such, they are prone to self-trauma.

PHARMACOLOGICAL CONSIDERATIONS FOR ANESTHESIA

This section is an overview of pharmacological agents that can be used for anesthesia of deer. Attention must be paid to hunting seasons and appropriate marking of wild captured animals, to avoid consumption of drug residues in meat.

Anesthesia of Captive or Game Farmed Deer

Game farmed and other captive deer often have very different drug requirements compared with free-ranging animals. The following section deals with anesthetic management of captive deer.

Sedation of Captive Deer White-tailed deer and mule deer usually require 2 to 3 mg/kg body weight (BW) of xylazine intramuscularly (IM) to produce recumbent sedation. Wapiti require approximately 1 mg/kg IM to produce recumbent sedation (Caulkett, 1997). Captive red deer may be sedated with 0.5 to 1 mg/kg of xylazine.

Once the xylazine has been administered, the animal should be left alone until it assumes a position of lateral recumbency or sternal recumbency with its head down. The deer can be cautiously approached and a towel should be placed over its eyes to decrease stimulation; noise should be kept to a minimum. Animals may appear to be very sedate under xylazine sedation, but they can rouse suddenly. To decrease the chance of sudden arousal, administer 1 mg/kg of ketamine into the jugular vein. Anesthesia can be maintained with 1 to 2 mg/kg of ketamine intravenously (IV), as required (generally at 10- to 15-minute intervals).

Yohimbine is effective in most cervids at a dose of 0.1 to 0.2 mg/kg BW. Administer 0.1 mg/kg IV and 0.1 mg/kg IM. Tolazoline is also effective, and can be used at a dose of 2 to 4 mg/kg.

Local Analgesia for Velvet Antler Removal The simplest way to block velvet antler is to perform a ring block at the base of the antler pedicle. Lidocaine HCl (without epinephrine) is administered at a dose rate of 1 ml/cm of pedicle circumference (Wilson et al., 2000). The block



Figure 53.2. Application of an antler ring block in an elk.

produces surgical analgesia in 1 to 2 minutes and lasts approximately 90 minutes (Figure 53.2).

Inhalational Anesthesia

Inhalational anesthesia is recommended for prolonged or very invasive procedures. Either halothane or isoflurane can be used. A small animal circle system can be used on animals weighing up to 150 kg. Use a 3- to 6-L rebreathing bag and fresh gas flows of 10 to 20 mL/kg BW per minute. Cervids premedicated with xylazine usually can be maintained on approximately 1% halothane or 1.3% isoflurane. Induction of captive adult cervids can often be achieved with xylazine sedation followed by IV ketamine at a dose of 2 to 3 mg/kg BW, using the techniques described. Xylazine-tiletaminezolazepam can also be used for induction. Fawns are usually easy to handle. Fawns can be induced with IV diazepam, 0.2 mg/kg, followed by 0.05 mg/kg of butorphanol IV, followed by 2 to 3 mg/kg of ketamine (Figure 53.3). Maintenance anesthesia of fawns can be achieved easily with volatile anesthetics and a small animal anesthetic machine.

Airway protective reflexes are absent underinhalational anesthesia, and regurgitation and aspiration can occur; therefore, intubation is recommended. Hypoventilation may be encountered, necessitating intermittent positive pressure ventilation. Usually, cervids maintain a relatively high blood pressure; hypotension may be encountered if ruminal tympany is present. The respiratory and hemodynamic compromise produced by ruminal tympany can be severe. The incidence of ruminal tympany can be decreased if food is withheld for 24 to 36 hours prior to anesthesia. Water should be withheld for 12 hours prior to anesthesia. Ruminal tympany may be resolved by passage of a stomach tube. If not, the anesthesia may be terminated, or emergency ruminal trocharization performed. Passive regurgitation can occur. Inflate the cuff on the endotracheal tube to ensure an adequate seal of the airway. The animal



Figure 53.3. Maintenance anesthesia of fawns can easily be achieved with volatile anesthetics and a small animal anesthetic machine.

should be extubated when the swallowing reflex occurs, and the ETT should be removed with the cuff partially inflated. Animals that have had xylazine premedication should receive yohimbine, to reverse the effects of the xylazine, at a dose of 0.1 to 0.2 mg/kg BW. Divide the dose; give half IM and half IV. Post-operative analgesia can be achieved with 0.025 to 0.05 mg/kg BW of butorphanol.

Capture of Free-Ranging Deer

Wild deer are generally at a greater risk for complications than captive deer. Drug requirements are higher and the risk of capture myopathy, hyperthermia, or trauma is potentially higher. There are a variety of protocols for the capture of deer. This section describes some of these protocols.

Xylazine-Tiletamine-Zolazepam Xylazine-tiletaminezolazepam is a useful mixture for the capture of wild deer (Janovsky et al., 2000; Murray et al., 2000) and for chemical immobilization and light anesthesia in game farmed or zoo animals. The effective dose for wapiti and moose is 1 mg/kg of xylazine + 2 mg/kg of telazol. White-tailed deer and mule deer require 1.5 mg/kg of xylazine + 3 mg/kg of telazol. Excited animals often require a higher dose. This combination provides approximately 45 minutes to 1 hour of anesthesia. Anesthesia may be prolonged with IV ketamine at a dose of 1 to 2 mg/kg every 15 minutes. Once the procedure has been completed antagonism of xylazine is recommended with tolazoline or yohimbine at the abovedosage. The major complication associated with this technique is hypoxemia. Read et al. conducted a trial to measure the respiratory effects of a xylazine/telazol mixture. All wapiti exhibited mild to marked hypoxemia ($PaO_2 = 43 \pm 11.8 \text{ mmHg}$) and showed marked improvement after 5 minutes of nasal insufflation of oxygen at 10 L/minute ($PaO_2 = 207 \pm 60 \text{ mmHg}$).

Medetomidine-Ketamine Medetomidine is a very useful α₂-agonist drug for wildlife anesthesia when it is formulated at a concentration of 10 mg/ml (zalopine). Medetomidine is 20 to 40 times more potent than xylazine. However, its use alone is not generally recommended as induction times are unacceptably long. Medetomidine is generally used in combination with ketamine. The major advantage of medetomidineketamine is that ketamine requirements are much lower than with xylazine. This factor allows for an earlier antagonism of the combination (i.e., the α_2 - agonist can be antagonized with less risk of unmasking convulsive activity or rigidity from residual ketamine). Hypoxemia and hypertension are the major complications that may be encountered with medetomidine-ketamine (Caulkett, Cribb, and Haigh, 2000). Medetomidine should always be antagonized with atipamezole at a 3 to 5:1 ratio. Less specific α_2 -agonist drugs (yohimbine, tolazoline) are usually not effective.

Potent Narcotics Potent opioids such as etorphine, carfentanil, and fentanyl have been widely used for immobilization of several different deer species (Haigh, 1990, 1991; Caulkett, Cribb, and Haigh, 2000; Moresco et al., 2001). In most cases they have been combined with Xylazine HCl, acepromazine maleate, or other sedatives to achieve optimum immobilization. The choice of opioid for use in deer may be governed as much by availability as by any other factor.

Thiafentanil oxalate (A3080, Wildlife Pharmaceuticals, Fort Collins, CO) is another potent opioid anesthetic that is being evaluated for wildlife and has been used in wapiti in a limited number of studies (Smith et al., 1993). Thiafentanil is approximately 6,000 times more potent than morphine, making it only slightly less potent than carfentanil, which is rated as 8,000 times more potent than morphine.

Doses in wapiti as high as $100 \,\mu\text{g/kg}$ provided very rapid immobilization (less than 1 minute in some cases) and numerous wapiti have been immobilized at doses near $50 \,\mu\text{g/kg}$ (Smith et al., 1993).

A variety of narcotic antagonists have been used in deer. They include nalorphine, diprenorphine (Revivon), naloxone (Narcan), nalmefene, and naltrexone (Trexonil).

Of these products, naloxone has the shortest halflife. Narcotic recycling, or renarcotization, especially of animals immobilized with carfentanil or etorphine, has been reported when naloxone is used (Haigh, 1991). Naltrexone is known to have a longer half-life in some species than any of the other antagonists listed (although no critical trials have been conducted in ungulates), and when adequate doses of naltrexone are used recycling is generally not a problem (Haigh, 1990).

Sedation of Free-Ranging Deer

Intranasal α_2 -Agonist Administration Intranasal drug administration has the advantages of a rapid onset time, reliability, and ease of administration. It is a useful technique to produce sedation in deer that are captured by physical means. Xylazine administered intranasally at a dose of 1.5 to 2 mg/kg produces reliable sedation and stress reduction in American elk (Cattet et al., 2004). Onset is rapid (often less than 1 minute), and the effects can be antagonized with yohimbine.

Neuroleptic Agents

Neuroleptics can be extremely useful in the management of wild and semi-domesticated deer. These drugs facilitate transport of deer and decrease stress in acutely captured deer. They have the potential to decrease the risk of trauma and capture myopathy. Azaperone (0.2 mg/kg) can be used immediately post-reversal to facilitate short translocations (6 hours or less). Zuclopenthixol acetate (1 mg/kg) provides up to 4 days of tranquilization (Read, Caulkett, and McCallister, 2000). Animals treated with this drug demonstrate decreased flight distance, decreased indices of stress, and improved water and food consumption compared to untreated animals (Read, Caulkett, and McCallister, 2000).

Anesthetic Protocols for Various Deer Species White-Tailed Deer (*Odocoileus virginianus*) and Mule Deer (*Odocoileus virginianus*) Mature white-tailed deer weigh 60 to 150 kg (Kreeger, Arnemo, and Rath, 2002). Mature mule deer weigh 75 to 135 kg. They are not difficult to anesthetize as long as they are kept calm during immobilization. Excited deer tend to override the sedative effects of α_2 -agonists and often require higher dosages for induction. Common complications include trauma, hyperthermia, and potentially capture myopathy. Ruminal tympany is not commonly encountered during anesthesia of these species. A variety of techniques have been used to induce immobilization. Hypoxemia is not uncommon and supplemental inspired oxygen should be considered.

White-tailed deer can be effectively anesthetized with 2.2 mg/kg of xylazine, combined with 4.4 mg/kg of Telazol (Murray et al., 2000). This combination is equally effective on mule deer, and immobilization can be partially antagonized with 0.1 to 0.2 mg/kg of yohimbine. Medetomidine at a dosage of 0.1 mg/kg, combined with 2.5 mg/kg of ketamine produces a good quality of immobilization in mule deer and white-tailed deer (Caulkett, Cribb, and Haigh, 2000). Atipamezole administered at three to five times the medetomidine dose effectively antagonizes immobilization.

North American Elk and Red Deer (*Cervus elaphus*) Elk or red deer may be captured via physical or chemical means. If physical capture (net gunning) is

used, sedation can be quickly induced with intranasal xylazine (Cattet et al., 2004). Mature Elk weigh 230 to 318 kg; red deer weigh 60 to 180 kg (Kreeger, Arnemo, and Rath, 2002). Chemical immobilization can be induced with narcotics or α_2 -agonists combined with dissociatives. Hypoxemia is common in anesthetized elk; it has been described during anesthesia with carfentanil-xylazine (Moresco et al., 2001). In this study, hypoxemia was effectively treated by partial antagonism of carfentanil with a low dose of naloxone. Hypoxemia has also been characterized during immobilization with xylazine-Telazol (Read et al., 2001). Elk can be immobilized with 10 µg/kg of carfentanil combined with 0.1 mg/kg of xylazine (Moresco et al., 2001). Immobilization should be antagonized with naltrexone. A mixture of 0.4 mg/kg of xylazine, combined with, 3 mg/kg of telazol is also effective (Millspaugh et al., 1995). Immobilization with this combination can be partially antagonized with 0.125 mg/kg of yohimbine.

Red deer are distributed throughout Europe; they are smaller than elk but considerations are similar. The drug of choice for red deer capture is 0.11 mg/kg of medetomidine, combined with 2.2 mg/kg of ketamine (Arnemo, Moe, and Søli, 1994). Medetomidine should be antagonized with 0.5 mg/kg of atipamezole. A good alternative is 2.5 mg/kg of xylazine, combined with 2.5 mg/kg of tiletamine-zolazepam (Janovsky et al., 2000). However, because of the long elimination time of tiletamine-zolazepam, recoveries are prolonged.

Moose (Alces alces)

Anesthesia of moose is very similar to anesthesia of other deer. One of the major complicating factors with moose is their large size. Mature moose can weigh 400 to 800 kg (Kreeger, Arnemo, and Rath, 2002). All of the same precautions apply, and particular attention must be paid to the prevention of capture myopathy and hyperthermia. There are several drug choices for anesthesia of moose. Carfentanil-xylazine has been advocated, as in other deer (Seal, Schnitt, and Peterson, 1985). The addition of xylazine to carfentanil decreases the incidence of muscle rigidity. Unfortunately, the addition of xylazine also increases the risk of regurgitation and aspiration pneumonia (Kreeger, 2000). For this reason, if carfentanil is used in moose, it should be administered as the sole agent at a dose of 10 µg/kg. In addition to the risk of regurgitation, they are at risk for hyperthermia and capture myopathy.

European moose have been effectively immobilized with 60 μ g/kg of medetomidine, combined with 1.5 mg/kg of ketamine (Arnemo, Soveri, and Søli, 1994). Immobilization can be antagonized with 0.3 mg/kg of atipamezole. Currently, the drug of choice for free-ranging moose is straight etorphine at a dose of 7.5 mg of etorphine per adult and half this dose in calves (Arnemo et al., 2004). We have also seen good results with xylazine-telazol in management situations. A dose of 1.5

mg/kg of xylazine combined with 3 mg/kg of telazol has proved effective. Immobilization can be partially antagonized with yohimbine or tolazoline.

Caribou and Reindeer (Rangifer tarandus)

Caribou often have high drug requirements when compared with other deer species. Their speed and agility can make them a difficult target for remote delivery. *Rangifer* sp. range in size from 80 to 300 kg (Kreeger, Arnemo, and Rath, 2002) with woodland caribou being the largest subspecies. The drug combination of choice for reindeer and caribou is 0.1 mg/kg of medetomidine plus 2.5 mg/kg of ketamine (Arnemo et al., 2000). This dose is not effective in free-ranging woodland caribou. In these animals, 0.2 to 0.25 mg/kg of medetomidine is recommended (Arnemo et al., 2000).

Fallow Deer (Dama dama)

Adult fallow weigh 40 to 100 kg. A variety of techniques have been used to anesthetize fallow deer, often with unreliable effects. Currently, the recommended drug combination for fallow deer is 0.1 mg/kg of medetomidine + 1 mg/kg of telazol (Fernandez-Moran, Palomeque, and Peinado, 2000).

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INTRODUCTION

The group of mammals referred to as antelope are a diverse collection of ruminants ranging from dik-dik to eland. Antelope are one of the groups of animals classically associated with game capture and translocation. Historically anesthesia in captive antelope was one of the veterinarians' most difficult challenges. Improvements in captive management, which include training techniques and the development of restraint devices, have decreased the need for anesthesia and have helped facilitate less stressful immobilizations. However, being skilled in antelope anesthesia will never totally be replaced with advances in restraint and training. Veterinarians with antelope in their care should strive to improve their anesthetic management.

TAXONOMY AND ANATOMY RELATED TO ANESTHESIA

Antelope is a common name given to various members of the family Antilocapridae and Bovidae. The pronghorn Antilocapra americana is the only member in the family Antilocapridae. The antelope are scattered in several subfamilies in the Bovidae. They are all ruminant Artiodactyla and range from a 3-kg dik-dik to 900-kg giant eland. There are several anatomical considerations to consider when anesthetizing antelope. The lack of upper incisors can help facilitate tracheal intubation but the depth of the larynx and the limitations in visualizing it can complicate intubation. The larynx itself is deep in the throat and difficult to visualize even with a laryngoscope and appropriate blade. One must ensure that there is an adequate depth of anesthesia before attempting to intubate an antelope, as excessive stimulation to the larynx can induce regurgitation.

The bovine lung is smaller, is divided into separate lobes, each with distinct lobules separated by complete septa. The diaphragm is more vertical and flatter in cattle

than in horses, and most of the bovine lung is cranial to the abdomen. A flatter conformation of the diaphragm results in decreased ventilatory efficiency (Pypendop, 2001). Tympany, regurgitation, and aspiration pneumonia are all serious potential complications when anesthetizing ruminants. The pharmacological effects of many anesthetics increase the chances of regurgitation. Recumbency (especially left lateral recumbency) increases tympany and regurgitation. This may be especially important in antelope that are darted for anesthetic induction and become malpositioned. The rumen occupies approximately three-fourths of the abdomen and may become distended when an antelope is recumbent. Increased intragastric pressure represents an additional unique pathophysiological condition for the diaphragm (Pypendop, 2001). With increased intragastric distention, a pattern of decreased respiratory rate and breath-holding at the end of inspiration is observed (Pypendop, 2004). Increased gastric pressure, gastric distention, and cranial displacement of the diaphragm can result in a significant decrease in lung dynamic compliance, tidal volume, and minute ventilation (Pypendop, 2001).

All large antelope should have adequate padding while recumbent. In dorsal recumbency, antelope should be balanced flat on their backs with the gluteal muscles sharing the weight and all limbs should be slightly flexed but relaxed. The neck needs to be supported as well to prevent hyperextension. Antelope in dorsal recumbency at any plane of anesthesia should be intubated. In lateral recumbency, there should be adequate padding for the radial nerve. To improve venous return an inner tube can be placed on the dependent forelimb and pulled cranial while the other limbs are lightly supported and moved perpendicular to the long axis of the body. The dependent eye must also be protected. The eye should be closed and padded with a towel or an inner tube. Most diagnostic procedures can be performed with the animal in sternal recumbency.

In a sternal position all four limbs should be tucked under the animal in a natural sitting posture. Flexing the head can have very serious consequences, as it will also reduce the airflow during respiration (Figure 54.1–54.2). It is the author's preference to keep the head extended and the airway as open as possible. If regurgitation is likely, then intubation is a better alternative than closing the airway.

BIOLOGY AND PHYSIOLOGY

The pronghorn is found only in western North America. The feet have two digits and the horns consist of a bony core covered with a keratinized sheath that is shed annually (Huffman, 1991). All antelope males and some females of certain species have unbranched horns attached to the frontal bones of the skull. The horns are

composed of a bony core and are covered with a keratin sheath that is never shed. As a general rule, antelope are herding animals and live in small groups to very large herds. All antelope are ruminants and spend a majority of a 24-hour period actively feeding or ruminating.

VASCULAR ACCESS SITES AND MONITORING

Over-the-needle catheters are often used in antelope veins. In areas in which the skin may be thicker, a cutdown with a scalpel or large gauge needle will facilitate catheter placement. Butterfly catheters can also be used

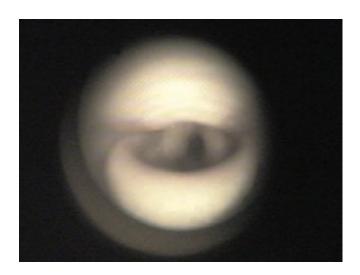




Figure 54.1. An endoscopic view of the epiglottis and glottis of an Arabian oryx with the head and neck slightly extended.





Figure 54.2. The same oryx and endoscope position as in Figure 54.1. The head is now flexed with the nose down, as is recommended to allow drainage of rumen reflux. The small black space at the bottom left of the picture is the open airway; the soft palate is displaced dorsally; and the epiglottis is pushing endoscope dorsally into the soft palate cranial to the laryngeal opening.

for shorter duration venous access or during emergencies. Common sites are the auricular, jugular, cephalic, medial and lateral saphenous, and lateral thoracic vein. Arterial access is most readily found in the radial, caudal auricular, and common digital arteries. The facial artery is palpable in most antelope species but can be difficult to catheterize in some species.

Several variables can be used to monitor the cardiovascular system, including heart rate, pulse strength, color of mucus membranes, and capillary refill time. Resting heart rates are generally not known in antelope species, but in domestic cattle resting heart rate is on average 80 beats per minute (bpm). Heart rate varies with size and age. Smaller ruminants have heart rates as high as 110 bpm (Riebold, 1996). Initial heart rates in darted animals or those that are physically restrained are likely to be significantly higher. The overall heart rate tends to drop as the anesthetic level deepens. Pulse pressure can be used in the field to estimate blood pressures indirectly. They can be evaluated at any of the sites mentioned for arterial catherization. Typically the strength of a palpated pulse decreases with depth of anesthesia. If digital pressure on the artery is easily accomplished during diastole, the arterial pressure can be assumed to be low (Riebold, 1996). Mucus membrane color should be pink in anesthetized antelope. The use of α_2 -agonists often makes the mucus membranes pale in color at the start of the anesthetic procedure. The colors will often return to a normal pink color after 20 to 30 minutes or if the α_2 drugs are antagonized. Capillary refill time should be less than 2 seconds, indicating good perfusion of peripheral tissues. Respiratory adequacy can be judged by monitoring respiratory rate and depth. Thoracic excursions or breaths felt from the nostrils are easy methods to monitor respiratory function. Ocular reflex and observation of eye position do not appear to be as useful in anesthetized antelope.

Monitoring core body temperature is essential in antelope anesthesia. Hyperthermia and subsequent capture myopathy are commonly encountered problems with antelope anesthesia. Placing a thermometer in the rectum is the most common location for temperature monitoring. Core temperatures may be better assessed with a flexible thermometer lead placed down the esophagus. Hyperthermia occurs most commonly during high ambient temperatures but can occur in temperature controlled environments. Common causes of hyperthermia include a prolonged induction, stress, and the depression of normal thermoregulatory mechanisms by anesthetic drugs. Under-dosing and poor dart placement with partial drug delivery inevitably lead to excessive pacing, capture stress, and resulting hyperthermia. Common approaches to treating hyperthermia in antelope have used topical water or cold water enemas. Another approach to cooling the patient is to deepen the anesthesia, intubate, and place the antelope

on a ventilator. This allows an exchange medium, oxygen and air, to contact a large surface and help dissipate heat. The ventilator also reduces the muscular effort required by the antelope. Paralytics can be used to quickly intubate and allow less resistance against the ventilator. Moderate intravenous (IV) fluid administration and non-steroidal anti-inflammatory drugs are useful adjuncts to this therapy. This approach has proved more successful in the author's hands than trying to cool the antelope externally, especially in larger species.

When anesthetic events in antelope are prolonged, as in a hospital setting, several additional anesthetic monitoring devices may be used to ensure the adequacy of the respiratory and cardiovascular systems. Pulse oximetry is now commonly employed in zoo animal anesthesia. Probes are typically placed on the tongue, ear, vulva, or prepuce. Reflectance probes can also be placed in the oral cavity against the gingiva, vaginally, or rectally. Indirect blood pressure can be measured with standard blood pressure cuffs. The tail and distal limbs are the most common sites for cuff placement. Blood pressures in sheep and goats should be maintained at 100 mmHg systolic, 60 mmHg diastolic with a mean of 75 mmHg, whereas cattle tend to have higher pressures normally (Riebold, 1996). These can serve as good guidelines for smaller and larger antelope, respectively. A mean of blood pressure 60 mmHg has been recommended as a minimum value for zoo bovids. Addax anesthetized with carfentanil, acepromazine and ketamine had initial mean arterial pressures of 118 mmHg (Klein, 1994). Addax that were anesthetized with carfentanil and xylazine had initial mean arterial pressures of 120.5 mmHg (Ball, unpublished data). Changes in blood pressure are often sensitive indicators in assessing the change in depth of anesthesia. Electrocardiography (ECG) can also be used in hospital settings. Lead placement can be a base-apex arrangement for large species or standard three-lead placement for smaller animals. Premature ventricular contractions (PVCs) are the most common arrhythmias seen in ruminants (Pypendop, 2001). Tracings of three or more PVCs are serious and warrant treatment. Common causes of PVCs include hypoxemia and hypercarbia. Administering lidocaine and correcting any underlying causes are essential. Arterial blood gases can also be used to monitor anesthesia.

INTUBATION

Intubation is recommended for any anesthetized antelope that needs to be transported or anesthetized for more than 1 hour. In species that are prone to regurgitation, such as giant eland, duiker, and addax, intubation should be considered during any anesthetic

event. It is advisable to be prepared to intubate antelope even during routine field procedures if complications arise. An adequate plane of anesthesia must be obtained before attempting to intubate. Blind intubation attempts are successful only about 50% of the time in cattle and are not recommended in antelope (Riebold, 1996). An effective technique for endotracheal intubation in antelope has been described (Bush, 1996). The larynx is visualized using a laryngoscope with a long straight blade. After visualization of the larynx a stylet or endotracheal tube exchanger (ETE) is placed into the trachea. With the laryngoscope removed the stylet or ETE can then be placed through the Murphy's eye of the endotracheal tube and the endotracheal tube is passed over the stylet and into the trachea.

REVIEW OF REPORTS ON ANTELOPE ANESTHESIA

Opioids have been the most commonly used class of drugs in antelope anesthesia. Recently, the potent opioid thiafentanil has been evaluated for antelope immobilization. Thiafentanil alone seems to have little advantage when compared with carfentanil. In impala immobilized with thiafentanil induction times and physiological parameters were comparable with values seen with the use of carfentanil (Jansen, 1991). The same authors successfully used thiafentanil to immobilize eland (Taurotragus oryx), greater kudu (Tragelaphus strepsiceros), and waterbuck (Kobus ellipsiprymnus). More trials have been conducted using thiafentanil in combination with medetomidine and ketamine. Roan antelope (Hippotragus equinus), free-ranging gemsbok (Oryx gazelle), boma confined Lichtenstein's hartebeest (Sigmoceros lichtensteinii), and boma combined and freeranging nyala (Tragelaphus angasii) have been successfully immobilized with combinations of thiafentanil, medetomidine, and ketamine (Citino, 2001, 2002; Grobler, 2001; Cooper, 2005). Naltrexone is used to antagonize thiafentanil at 30 mg of naltrexone per 1 mg of thiafentanil given either intramuscularly (IM) or intravenously (IV). Atipamezole is given IM to antagonize the medetomidine. In one study, free-ranging pronghorn (Antilocapra americana) were anesthetized with thiafentanil and xylazine. This combination was judged to be superior to previously used anesthetic combinations in pronghorns (Kreeger, 2001).

Carfentanil and etorphine are still the most commonly used opioids for antelope anesthesia. Opioids are often combined with α_2 -agonists or tranquilizers when anesthetizing antelope. The benefits of these combinations include lowering the narcotic dose, using smaller drug volumes, shorter induction times, and better muscle relaxation than with the opioid alone. Table 54.1 lists carfentanil and xylazine combinations used in antelope by the author. In some species, etorphine in

combination with xylazine may have a better quality of anesthesia and shorter recovery times (Howard, 2004). Detomidine has been used in addax and blue wildebeest in combination with opioids (Portas, 2003) (Table 54.1). Arabian and Scimitar horned oryx have been anesthetized for long periods with combinations of etorphine and medetomidine, and there were fewer complications with this combination when compared with carfentanil and xylazine (Ancrenaz, 1996) (Table 54.1).

A 1:1 mixture of xylazine and ketamine added to etorphine (M-99KX) was found to lower the narcotic dose by as much as 30% and provide better overall anesthesia than etorphine and xylazine (Snyder, 1992). Anesthesia in captive bongo was found to be superior with carfentanil-ketamine-xylazine (CKX) in combination versus either carfentanil alone or carfentanil and acepromazine together (Miller-Edge, 1994). Carfentanil and xylazine combinations causes hypoxemia and hypertension in captive bongo, and blood gas analysis is useful during anethesia with these drugs (Schumacher, 1997).

Alternative drug combinations can be used in antelope if potent opioids are not available. Tiletaminezolazepam in combination with butorphanol and an α₂-agonist has been used in addax (Addax nasomaculatus), eland (Taurotragus oryx), scimitar-horned oryx (Oryx dammah), impala (Aepyceros melampus), wildebeest (Connochaetes taurinus), and blackbuck antelope (Antilope cervicapra) (Paras, 2002). Induction was faster with the xylazine-tiletamine-zolazepam-butorphanol combination than with the medetomidine-tiletaminezolazepam-butorphanol combination. The xylazine-tiletamine-zolazepam-butorphanol combination appeared to have a shorter duration of effect, and some animals were aroused suddenly during handling. The detomidine-tiletamine-zolazepam-butorphanol combination had the longest duration of action. Tiletamine-zolazepam and xylazine has been used to immobilize captive sable antelope, scimitar-horned oryx, and Arabian oryx (Bush, 1992). Disadvantages with this combination were prolonged and stormy recoveries, hypersalivation, and some muscle rigidity. Doxapram hydrochloride appeared to hasten recovery in several of the antelope immobilized with this combination.

Ketamine and medetomidine combinations have been investigated in antelope in recent years. Addax have been successfully immobilized with medetomidine and ketamine (Portas, 2003). Ketamine and medetomidine in combination were effective for immobilizing captive impala (*Aepyceros melampus*) (Phillips, 1998). Ketamine and medetomidine in combination are the preferred drugs for immobilizing captive gerenuk. They can be delivered by dart or often times captive gerenuk are manually restrained and immobilizing drugs can be given IV or IM. Atipamezole is given to antagonize the medetomidine usually it is administered IM or one-half of the dose IV and one-half IM.

Table 54.1. Anesthetic induction regimens for selected antelope species with average adult captive body weights.

Impala (Aepyceros Melampus)

Males 57 kg, female 42 kg

30 µg/kg carfentanil and 0.2 mg/kg xylazine

Use lower dose of xylazine in this species as respiratory depression can be significant

Greater Kudu (Tragelaphus Strepsiceros)

Male 210 kg, female 149 kg

26 µg/kg carfentanil and 0.26 mg/kg xylazine

Higher dose of narcotic reduces pacing but still a common finding

Defassa Waterbuck (Kobus Ellipsiprymnus Defassa)

Male 215 kg, female 177 kg

22 µg/kg carfentanil and 0.22 mg/kg xylazine

Nervous species, prone to prolonged induction. Tough skin, dart placement critical. Recommend use of hyaluronidase. Obesity also common.

Blue Wildebeest (Connochaetes Taurinus)

Male 182 kg, female 142 kg

21 µg/kg carfentanil and 0.21 mg/kg xylazine

 $32 \mu g/kg$ etorphine and $40 \mu g/kg$ detomidine

Herd members can be aggressive to narcotized animal. Tends to be obese in captivity and hence prone to hyperthermia.

Uganda Kob (Kobus Kob)

Male 100 kg, female 62 kg

35 µg/kg carfentanil and 0.35 mg/kg xylazine

Flighty species. Prone to excessive running after darting. Quick induction required to help avoid hyperthermia.

Sable Antelope (Hippotragus Niger)

Male 265 kg, female 166 kg

 $17.5 \,\mu g/kg$ and $0.17 \,mg/kg$ xylazine

Dangerous when under-dosed. Heavily muscled and can be obese in captivity; prone to hyperthermia. Hyaluronidase useful

Roan Antelope (Hippotragus Equinus)

Male 310 kg, female 235 kg

 $18\,\mu\text{g}/\text{kg}$ carfentanil and 0.18 mg/kg xylazine

Dangerous when under-dosed. Heavily muscled and often obese in captivity; prone to hyperthermia. Hyaluronidase useful.

Common Eland (Taurotragus Oryx)

Male 570 kg, female $300 \, kg$

16 μg/kg carfentanil and 0.16 mg/kg xylazine

Can be dangerous when under-dosed. Incredible leaping ability. Males are heavily muscled; excessive pacing will lead to hyperthermia. Be prepared to supplement or recover about 20 minutes into the anesthesia.

Bongo (Tragelaphus Eurycerus)

Male 410 kg, female 249 kg

 $24\,\mu\text{g/kg}$ carfentanil and 0.24 mg/kg xylazine

Typically sedate animals but good leapers.

Scimitar-Horned Oryx (Oryx Dammah)

Male 180 kg, female 123 kg

29 µg/kg carfentanil and 0.29 mg/kg xylazine

56 μg/kg etorphine and 5 μg/kg medetomidine

Renarcotization more common with carfentanil. Tends to be obese and prone to hyperthermia.

Arabian Oryx (Oryx Leucoryx)

Male 102 kg, female 89 kg

37.5 μg/kg carfentanil and 0.25 mg/kg xylazine

48.5 μg/kg etorphine and 48.5 μg/kg detomidine

Etorphine recommended over carfentanil due to renarcotization. More slender and delicate in structure than scimitar horned but tends to be obese in captivity.

Addax (Addax nasomaculatus)

Male 108 kg, female 88 kg

 $22.7\,\mu\text{g/kg}$ carfentanil and $0.22\,\text{mg/kg}$ xylazine

Table 54.1. (Continued)

Moderate amount of renarcotization if higher dose of carfentanil used. Etorphine is likely a better choice but limited experience to report.

Bontebok (Damaliscus Pygargus)

Male 80 kg, female 58 kg

 $25 \,\mu\text{g/kg}$ carfentanil and $0.25 \,\text{mg/kg}$ xylazine

Can be difficult to dart, runs excessively afterward. Prone to hyperthermia. Hyaluronidase recommended; doses even higher than those listed (40 µg/kg) should be considered for very quick recumbency in large pens.

Sitatunga (Tragelaphus Spekii)

Male 85 kg, female 58 kg

40 µg/kg carfentanil and 0.30 mg/kg xylazine

Can be dangerous kickers when recumbent. Hyaluronidase highly recommended. Higher doses useful for quicker recumbency.

Tends to run and moderate risk of regurgitation. Will run into

Nyala (Tragelaphus Angasii)

Male 105 kg, female 63 kg

28.5 μg/kg carfentanil and 0.25 mg/kg xylazine

Very shy and nervous

Gerenuk (Litocranius walleri)

Male 30 kg, female 25–30 kg

 $1.5-2.0 \, mg/kg$ ketamine and $0.06 \, mg/kg$ medetomidine Nervous and fragile.

STRATEGIES FOR FIELD CAPTURE AND ANESTHESIA IN REMOTE LOCATIONS

The evolution of capture and field anesthesia in antelope species has been well documented (McKenzie, 1993). South African veterinarians have been at the forefront of this development and continue to set standards for wildlife capture. Although better drug combinations and drug delivery systems have made field anesthesia safer for both humans and antelope, the importance of well-organized capture procedures cannot be underestimated. The veterinarian overseeing such operations has the welfare of the antelope and the safety of staff as a priority. Many antelope species can be captured with mass capture techniques. In these instances sedation or tranquilization can be used in select species. Quick, smooth, efficient captures are the key to avoiding animal losses during mass captures and facilitate the effectiveness of tranquilization. Proper placement of the capture boma and using a skilled helicopter pilot to drive the antelope into the boma are critical. Tranquilizers and sedatives commonly used by the South African National Parks (SANParks) are listed in Table 54.2.

Field anesthesia of individuals is less common but still occurs in free-ranging animals and in bomaconfined animals. Smooth and quick inductions are desirable when anesthetizing antelope. Depending on the scenario, darting from the ground or a helicopter may be indicated. Animals should not be chased for more than 2 minutes prior to darting. This may help reduce the incidence of hyperthermia and stress-related complications. Darting techniques and equipment

Table 54.2. Drugs used by SANParks in the mass capture of various species.

					Tranqui	lizers and Sec	latives			
		Haloperidol (mg)		Perphenazine enanthate (mg)			Diazepam (mg)			
Species Route		AM	AF	SA/J	AM	AF	SA/J	AM	AF	SA/J
Eland	IM	25	20	14-18	100	80	40-60	25	20	14-18
Kudu	IM	15	10	6-8	60	40		15	10	
Gemsbok	IM	10	8					20	15	
Roan	IM	12	10		60-80	40-60		15	12	
Sable	IM	14	12		60-80	40-60		14	12	
Waterbuck	IM	20	15		60-80	40-60		20	15	
Blue Wildebeest	IM	14	12	6-8	60-80	40-60		20	15	
Black Wildebeest	IM/IV	14	12	6-8	60-80	40-60		14	12	
Red Hartebeest	IM/IV	16	14	6-8	60-80	40-60		16	14	
Tsessebe	IV	15	15	7	60-80	40-60		15	15	7
Blesbok	IV	12	12	6	50	40		12	12	6
Bontebok	IV	12	12	6	50	40		12	12	6
Impala	IV			6				14	12	6
Grey reedbuck	IV	8	8	4				8	8	4
Mountain reedbuck	IV	10	10	5				10	10	5
Springbok (Kalahari)	IV	14	12	7	40-60	40		14	12	6
Springbok (Karoo)	IV	12	10	5	40-60	40		12	10	5
Klipspringer	IV	5	5	3				5	5	3
Steenbok	IV	5	5	3				5	5	3
Duiker	IV	8	8	4				8	8	4

The abbreviations used in the column headings indicate the different age classes as follows: AF, Adult female; AM, adult male; SA/J, sub-adult or juvenile.

The above doses are for wild animals in good condition.

Animals that are in poor condition tend to show greater sedation and often develop extra-pyramidal symptoms (EPS).

Diazepam is the drug of choice to treat EPS.

Diazepam has a shorter duration of action, and it may necessary that it be repeated after a few hours.

are covered in the chapter on remote drug delivery. Table 54.2 lists the species and drugs doses that are commonly handled by SANParks.

GUIDELINES FOR ANESTHESIA IN SPECIFIC ANTELOPE SPECIES

Anesthesia Planning and Preparations

The goal of the anesthetic procedure (routine examination, diagnostic tests, and transportation) should be detailed well enough so that it moves forward efficiently. Equipment that are needed to move the antelope should be available in case of emergency. Staff should be briefed and given specific responsibilities for the procedure. A checklist of basic equipment needs is useful for every anesthetic procedure and should be developed based on the individual needs, preferences, and goals of the procedures themselves. Routine equipment needed for antelope anesthesia include ropes, blindfolds, inner tubes, towels, slings, and ear plugs. Portable scales are important to get accurate body weights when possible. Medical equipment should consist of an endotracheal intubation kit or nasal insufflation equipment, demand valves, an oxygen supply, IV access kits, fluids, and emergency drugs. Monitoring equipment for field procedures should be a stethoscope and a thermometer at a minimum. Portable pulse oximeters are now readily available and a highly recommended piece of equipment for all anesthetic events.

A review of previous anesthesia records is an excellent opportunity to critically examine previous procedures. Accurate and organized medical records make critical evaluation much easier. For major procedures, a planning session with all parties involved also makes for a smoother anesthetic episode. Most adult ruminants should be fasted for 18 to 24 hours prior to anesthesia. Fasting can induce bradycardia and even prolonged fasting does not ensure that the antelope will not regurgitate (Riebold, 1996). It is the author's preference to only remove any concentrate ration from the diet and allow access to hay, grass, and water. The propensity for certain species to regurgitate, such as duikers, addax, and eland, may be the result of a subclinical rumenitis. Isolation may stress an individual prior to anesthetic induction. An anesthetic procedure will have a less significant impact on the antelope and its herd if the environmental conditions are kept as normal as possible for that animal.

ANESTHETIC REGIMENS FOR ANTELOPE IN MANAGED CARE

An extensive review of chemical restraint regimens was recently provided for numerous antelope species

Table 54.3. Drugs used in South African National Parks for the immobilization of various antelope species.

	Immobilizing Drug Mixture					
	Etorph	ine (mg)	Azaperone (mg)			
Species	Adult Male	Adult Female	Adult Male	Adult Female		
Sable	4-5	3-4	100	100		
Roan	4-5	3-4	100	100		
Blue wildebeest	4-5	3-4	100	100		
Black wildebeest	3-4	3	80	80		
Tsessebe	3-4	3	80	80		
Eland	10-12	6-8	180-200	180-200		
Red hartebeest	4-5	3–4	80	80		
Gemsbok	4-5	3-4	80	80		
Kudu	5-6	4-5	100	100		
Waterbuck	5-6	4–5	150	150		

All doses should be administered intramuscularly.

Diprenorphine at 2.5 times the etorphine dose in mg.

Naltrexone at 15 times the etorphine dose in mg.

Hyaluronidase is frequently added to the immobilizing drugs to assist drug absorption and thereby reduce the induction time.

(Citino, 2003). Table 54.1 provides data collected from various facilities from 1996 to 2006 by the author. In general a 1-mg:10-mg cocktail of carfentanil to xylazine is used routinely for most species of antelope. Most doses of narcotics listed in Table 54.3 are somewhat higher than those commonly reported. With these doses induction times are quick and the antelope are typically immobilized in a few minutes. Adequate support should be available for animals immobilized in quick fashion. Naltrexone is used to antagonize the carfentanil at 100 times the carfentanil dose, on a per milligram basis split one-half IV and one-half IM. Xylazine is not routinely antagonized and it will provide some post-anesthetic tranquilization. Xylazine causes some sedation and animals are readily accepted back into the herds after the procedure.

INDUCTION

Prior to any antelope anesthetic induction, the veterinarian must ensure that there is adequate support staff and necessary equipment. All anesthetic inductions need to be carried out in a calm, quiet environment to lessen any stress on the antelope. The purpose of the anesthetic procedure may dictate the level of anesthesia needed and perhaps even the choice of drugs used. This may also figure into the delivery method of the induction dose. The delivery of the induction dose should be smooth, quick, and as controlled as possible to minimize stress.

Anesthetic induction can take place with an antelope physically restrained or in a confined space. Most anesthetic inductions in antelope are delivered from a remote delivery system or dart. Dart placement is critical, and personnel experienced with the use of darting equipment should dart the antelope. The muscle masses of the shoulder, neck, and upper hind leg are ideal targets

for dart placement. Adequate velocity on the dart is needed to ensure deep IM injections. Incomplete or slow inductions can occur if the dart is placed in subcutaneous (SC) tissue, or in intraperitoneal or intrathoracic spaces. Incomplete drug delivery and slow inductions can cause the animal to pace excessively and become hyperthermic. The antelope's skin thickness should be considered when selecting the length of dart needles and also what dart velocity is used to deliver the dart. Poor dart placement contributed to a 30 percent anesthetic related mortality in a herd of captive Defassa Waterbuck (Kobus ellipsiprymnus) (Ball, unpublished data). All animals had prolonged induction times and died as a result of complications from hyperthermia. Waterbuck that received the same doses in the muscle mass of the hind limb had unremarkable anesthetic events. Obese animals in captivity may also have prolonged inductions because of the injection of drug into fatty tissue. The addition of hyaluronidase to the induction drugs can reduce induction times and is especially important in obese animals and those with thick skin. Once the antelope is safe to approach it should be blindfolded to decrease stimulus. Earplugs may be considered to decrease auditory stimulus. If the antelope is not recumbent, it should be blindfolded and can be eased into recumbency. If the antelope is not intubated, then intranasal oxygen can be given and routine monitoring can begin.

Advances in physical restraint systems for antelope can allow for hand injection of induction agents and in certain cases induction drugs can be administered IV (Atkinson, 1999; Wirtu, 2005). Reduced doses of induction drugs can be used IM or IV if the antelope is physically restrained. Nyala have been successfully anesthetized in a drop chute system (The Tamer, Fauna Products Inc., Red Hook, NY) with IV ketamine (4 mg/kg), medetomidine (8 μ g/kg), and butorphanol (0.3 mg/kg) in combination prior to euthanasia

(Ball, unpublished data). Supplemental induction doses may be needed at times in either remote delivery situations or once the antelope is handled. If remotely delivered supplemental drug dosing is required, another full induction dose of the narcotic drug is usually given. Once control of the antelope has been obtained, the clinician can determine if it is safe to proceed or antagonize the entire narcotic dose and recover the animal. If the antelope is restrained and needs supplemental dosing, IV ketamine 0.5 to 1 mg/kg can be given to facilitate better control or allow intubation. Higher doses of ketamine can be given but the antelope may become apneic and need respiratory support. Ketamine is metabolized relatively quickly but the narcotic antagonist should not be given for at least 20 minutes after ketamine administration to allow a smooth recovery.

Capture myopathy is a potentially life-threatening complication resulting from prolonged induction or inadequate induction. Capture myopathy is also more specifically termed exertional rhabdomyolysis in wildlife capture and anesthesia. Four clinical syndromes are described: acute death syndrome, delayed peracute death, ataxic-myoglobinuric syndrome, and muscle rupture syndrome (Neilsen, 1999). The acute death syndrome occurs within a few hours of the anesthetic event and often the antelope expires during the anesthesia. The most notable clinical finding in the author's experience is pronounced hyperkalemia. If immediate electrolyte analysis is not possible, an ECG tracing may suggest hyperkalemia in antelope. Corrective measures for hyperkalemia include administering calcium gluconate as a cardioprotective agent. Giving insulin and dextrose to stabilize the potassium levels may follow calcium administration. After lowering the potassium levels, the inciting causes of the hyperkalemia (hyperthermia, lactic acidosis, etc.) can be addressed. The delayed peracute syndrome occurs within 24 hours and is believed to result from the effect of hyperkalemia on the myocardium. The third syndrome is the ataxicmyoglobinuric syndrome, which may occur within several days from the anesthesia. The urine is often brownish-red in color; and muscle, liver, and renal enzymes are typically elevated. Death is usually from renal failure associated with the myoglobinuria. Some animals recover spontaneously with adequate fluid therapy. In some selected cases, dobutamine can be given IV to increase renal perfusion (Ball, unpublished data). Dantrolene is used in equine patients with post-anesthetic myositis and may be considered in antelope that are experiencing complications of capture myopathy.

RECOVERY

A major advantage of opioid induction is the ability to antagonize the drugs and produce a smooth recovery. Naltrexone is the preferred antagonist and can be administered at 100 times the carfentanil dose or 15 times the

etorphine dose. The dose is often split among IV, IM, and SC administration. The product label recommends giving one-fourths of the dose IV and three-fourths SC. A recent study in goats suggests that there is no advantage to splitting the dose when antagonizing carfentanil (Mutlow, 2004). Mild renarcotization was noted in many of the study animals. Although renarcotization is not fully understood, there appear to be more episodes of renarcotization in antelope species from arid climates. Water conservation mechanisms in these species may have a role, but this has not been investigated.

Recovered animals can be placed back into the herd immediately if conspecifics do not pose a threat to the recovering animal. Once the opioid fraction of the induction is antagonized, recovery generally takes a few minutes. In most circumstances the sedative drug is not antagonized. The sedative may keep the recovering antelope calmer. Arousing from anesthesia can be a startling experience for antelope and may be stressful for the animal. A calm slow recovery is the preferable way to recover an antelope. Antelope that have been under inhalation anesthesia should be recovered away from other animals. Opioid antagonists are not given until the anesthetic gas can no longer be detected from the endotracheal tube. The tube is left in place until a strong swallowing reflex is seen. The cuff is only slightly deflated to help clear the airway of any regurgitated material.

ANESTHESIA RECORDS

An accurate record of the anesthetic procedure is essential. Anesthetic records allow the creation of a data base that can be critically evaluated and used as a reference. Drug delivery, dosages, drug effects, physiological data, and the notation of complications are important parts of an anesthetic record. A dedicated person should be assigned to record this information. Compilation into an electronic record keeping system is also a valuable tool for planning future events.

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55

Gazelles

Gary West

INTRODUCTION

There are 16 species in the genus *Gazella*. Table 55.1 lists those species commonly kept in captivity and normal adult body weights. Gazelles are often nervous, making handling and capture difficult. Immobilization is often necessary to perform basic procedures such as hoof trimming or disease testing. General anesthesia is usually required for even minor surgical procedures. Basic cardiopulmonary physiology and anesthetic monitoring in gazelles is similar to small domestic ruminants (Riebold, 1996). Published reports on anesthetic monitoring and support in small domestic ruminants can be consulted for these species.

PRE-ANESTHETIC PREPARATIONS

Gazelles often mask underlying disease and obtaining pre-immobilization diagnostic blood work is usually not feasible. Even severe disease conditions (e.g., renal disease resulting from medullary amyloidosis) can be difficult to assess pre-immobilization (Wallace, 1987; Duncan, 1997). It is not possible to completely fast these species when they are maintained in large outdoor exhibits and isolating or confining gazelles to a barn is often stressful. Different methods of capture and their effects on blood parameters have been evaluated (Rietkerk, 1994). Animals caught quickly or confined for

Table 55.1. Normal adult body weights of select Gazelle species.

Thomson's gazelle, Gazella thomsoni	20-27 kg
Mountain gazelle, Gazella gazella	20-50 kg
Slender-horned gazelle, Gazella leptoceros	20-30 kg
Addra gazelle, Gazelle addra	40-80 kg
Dorcas gazelle, Gazella dorcas	20-30 kg
Grant's gazelle, Gazella granti	35-80 kg
Soemmering's gazelle, Gazella soemmeringi	35-45 kg
Speke's gazelle, Gazella spekei	13-25 kg
Goitered gazelle, Gazella subgutturosa	18-30 kg

short periods of time undergo much less stress than those confined for several hours prior to handling (Rietkerk, 1994). Some institutions can handle and confine their gazelles to small barns or corrals and may get them into small squeeze crates immediately before the immobilization. Free ranging or semi-free ranging animals may be driven into corrals or bomas for handling or darting.

Fasting may reduce complications such as tympany, regurgitation, and aspiration pneumonia. Ideally, food and water should be withheld for 12 to 24 hours. Fasting for longer than 24 hours has been associated with metabolic acidemia in small domestic ruminants and is not recommended (Gray, 1986). Extended fasting may also promote liquid ingesta formation and increase the possibility of regurgitation (Gray, 1986).

PHYSICAL RESTRAINT

Many gazelles can be hand caught by experienced staff and immobilizing drugs can be administered subsequently. For physical capture, animals are restricted to a small enclosure or barn. The initial phase of hand capture is the most critical to minimize self-inflicted trauma. The horns of the gazelle are grabbed first, and the animal is quickly lifted off of its feet while the body is supported and the legs are restrained. An experienced handler can hold the horns and head with one arm, while partially supporting the neck and torso with the other arm. An additional handler can restrain and support the hind part of the body and restrain the legs. Larger gazelles may require more than two people for safe and proper restraint. In addition to puncture wounds from the horns, potential injury to handlers can also come from their sharp hooves. Nets can be used, but are potentially dangerous for the animal. Legs can become entangled and injured as the animal struggles excessively before being manually restrained. Some species of gazelle are considerably more docile then others. The dama or addra gazelle (Gazella dama)

can often be manually restrained by grabbing the horns and pushing the animal into sternal recumbency with two or three handlers. This technique works best in a dark barn with minimal noise. The use of blindfolds may help keep animals calm.

Handlers must consider acute stress as a cause for sudden death, and should handle an animal expeditiously. Sudden death could potentially occur in debilitated animals because of arrhythmias caused by sudden catecholamine release (Gray, 1986). Capture of free-ranging gazelles may be done by driving the gazelles into bomas and further confining them with the use of canvas screens (Rietkerk, 1994). However, holding animals in bomas for several hours prior to handling will likely increase stress-related complications (Rietkerk, 1994).

INDUCTION

Gazelles that are manually restrained can be masked down with isoflurane or sevoflurane. The addition of nitrous oxide may speed induction, but its use causes gaseous distention of the forestomachs when used for prolonged periods. In manually restrained gazelles, induction may also be accomplished with intravenous administration of propofol, ketamine/midazolam, tiletamine/zolazepam, or ketamine/medetomidine (Table 55.2).

Handling systems and chutes may be part of the animal's exhibit. They may be confined to these chutes and hand injected intramuscularly (IM). If gazelles are kept in holding pens or smaller exhibits, they are often darted IM with lightweight, low-impact, plastic projectile darts (see Chapter 4). Some gazelles (e.g., Grant's gazelles) only allow human approach up to a specific distance, making darting very challenging. Hide blinds or darting from familiar vehicles may make animals less agitated and easier to approach. Some species stay in perpetual motion (running or pacing) once pursued, making it virtually impossible to fire a dart at a stationary target. Small-volume projectile darts are critical in these situations. This author has found the Pneudart to be a very effective and accurate projectile

Table 55.2. Doses of anesthetic induction agents used in gazelles.

Propofol	4–6 mg/kg IV
Ketamine + midazolam	4 mg/kg (K) + 0.2 mg/kg (Mi) IV
Tiletamine/zolazepam	2–4 mg/kg IV
Ketamine +	4 mg/kg (K) + 0.05 mg/kg (M) IV
medetomidine	
Ketamine	1-2 mg/kg IV as supplemental
	anesthesia
Carfentanil	0.018-0.022 mg/kg IM
Carfentanil + xylazine	$0.02 \text{ mg/kg} (C) + 0.2-0.5 \text{ mg/kg} (X) \text{ IM}^*$
Medetomidine +	0.04-0.07 mg/kg (M) + 2-4 mg/kg (K) +
ketamine +	$0.2-0.4 \text{ mg/kg (B) IM}^*$
butorphanol	

^{*}Preferred combinations.

for long distance darting. However, these darts may cause extensive tissue damage (Cattet, 2004).

Drug combinations for intramuscular induction include opioid/ $\alpha 2$ -adrenergic agonist, cyclohexamine/ $\alpha 2$ -adrenergic agonists with benzodiazepines or opioids, or opioid/butyrophenone combinations. This author's preferred induction regimen is carfentanil with an $\alpha 2$ -adrenergic agonist such as xylazine. This combination allows a small injection volume, rapid induction, and mild cardiopulmonary side effects. It is very useful for short procedures or when darting animals from long distances. Ketamine can be given intravenously (IV) as an anesthetic supplement if needed. Once the gazelle becomes recumbent wait 5 to 10 minutes before approaching to allow the xylazine to reach maximum effect and further relax the animal (Allen, 1991).

Carfentanil alone is effective for induction, but it produces bradycardia and hypertension (Schumacher, 1997). Antagonism is accomplished with naltrexone (100 mg/mg carfentanil, IV or IM) (Mutlow, 2004). Xylazine is antagonized with either tolazoline or atipamezole (Table 55.3). Yohimbine may also be used as a low-cost alternative to reverse xylazine effects, but it is less specific and less effective.

A combination of medetomidine, ketamine, and butorphanol (Table 55.2) has been evaluated in Thompson's gazelles (Gazella thomsoni) (Chittick, 2001). The gazelles were confined to a chute and hand injected. Catheterization of peripheral arteries was not successful probably because of peripheral vasoconstriction caused by medetomidine (Chittick, 2001). Gazelles immobilized with this combination are usually under light anesthesia. If painful procedures are performed, supplementation to reach general anesthesia or local anesthetic techniques should be used (Chittick, 2001). Disadvantages of this combination include bradycardia, transient hypertension, hypoxemia, respiratory acidemia, long inductions, and the relatively large volumes needed for induction (Chittick, 2001). This combination is most effective when gazelles are confined to a barn or chute because of prolonged induction times. This combination is partially reversed with atipamezole and naloxone (Table 55.3).

Ketamine and xylazine has been used to capture free and semi-free living gazelles as an alternative to potent narcotics (Foster, 1999). Previous captures using etorphine combinations resulted in significant post-capture mortality (Foster, 1999; Molnar, 2002). Physiological monitoring in response to ketamine and xylazine immobilization was limited to body temperatures,

Table 55.3. Doses for anesthetic antagonists used in gazelles.

Naltrexone	100 mg per 1 mg carfentanil IM or IV
Atipamezole	0.1 mg/kg IM to reverse alpha ₂ -agonists
Naloxone	0.01–0.02 mg/kg IV or IM
Tolazoline	0.5-1.0 mg/kg IV of IW $0.5-1.0 \text{ mg/kg IM to reverse alpha}_2$ -agonists

pulse, and respiratory rates. Therefore, the effects of this combination are difficult to evaluate based on the monitoring that was done. The study states that there were no serious changes in heart or respiratory rate, but these values alone are not sufficient to evaluate cardiopulmonary status of the animals. Also, in this author's experience, and when compared with other studies in gazelles (Schumacher, 1997; Chittick, 2001), these animals apparently exhibited both bradycardia and bradypnea. Five of 58 animals died within 3 days of capture from capture myopathy, aspiration pneumonia, trauma, or enteritis.

A combination of fentanyl/azaperone immobilized mountain gazelles in large enclosures (Greth, 1993), allowing handling and blood collection. The addition of promethazine appeared to improve quality of relaxation (Greth, 1993). No post-capture mortality was seen the beneficial effects of azaperone (i.e., less fear of humans and some mild sedation) were seen post-handling (Greth, 1993).

Tiletamine-zolazepam in combination with either an $\alpha 2$ -adrenergic agonist (medetomidine or xylazine) or butorphanol may also be used. This combination has not been specifically studied in gazelles but has been used in other non-domestic bovids (Bush, 1992). Disadvantages include longer induction and recovery times and hypoxemia (Bush, 1992). Tiletamine-zolazepam and butorphanol combinations have less severe cardiopulmonary alterations in ruminants than tiletamine-zolazepam combinations with an $\alpha 2$ -adrenergic agonist (Howard, 1990). These combinations are better after an animal has been physically restrained and the combinations are administered intravenously. Doxapram can hasten the recovery process in animals given $\alpha 2$ -agonists (Bush, 1992; Riebold, 1996).

Etorphine, in combination with ketamine and xylazine, or with azaperone, has been used successfully to immobilize gazelles (Snyder, 1992; Molnar, 2003). Etorphine with ketamine/xylazine has the advantages of lowering the opioid dose by 30%, increasing analgesia, shortening induction times, and decreasing problems with renarcotization (Snyder, 1992). Etorphine in combination with azaperone was used to capture gazelles in field conditions (Foster, 1999; Molnar, 2002). Hyperthermia, capture myopathy, and aspiration contributed to morbidity and mortality. The study concluded that when capturing these species in high ambient temperature conditions, the use of ketamine and xylazine combinations might be a better choice (Foster, 1999; Molnar, 2002).

MAINTENANCE

Anesthesia can be maintained with isoflurane or sevoflurane. Gazelles should be intubated if the immobilization procedure will be greater than 20 minutes. This helps prevent aspiration of ingesta and hypoxemia.

To intubate a gazelle, the head is hyperextended and the maxilla is held open with rolled gauze or similar. Straight positioning of the neck and head is critical, in part because of the narrow mouths of gazelle species. The tongue is pulled laterally and the pharyngeal area may be cleared of secretions by swabbing. A flat laryngoscope blade, 20 to 35 cm long, is commonly used to facilitate visualization of the larynx. Alternatively, intubation can be done "blindly" by using one hand externally and ventrally to manipulate and position the larynx while using the other hand to guide and advance the endotracheal tube. Lidocaine applied to the larynx may help obtund laryngospasm that may occur. The gazelle should be relaxed prior to attempting intubation to help avoid laryngospasm and regurgitation. Often induction protocols have to be further supplemented by masking the gazelle with inhalant anesthetics prior to attempting intubation.

Adult gazelles are typically intubated with 6- to 12-mm endotracheal tubes. A stylet or polypropylene urinary catheter may be placed first and the endotracheal tube then slid over it into the tracheal lumen. Confirmation of intubation can be done by checking for condensation in the tube, feeling respirations, moving of the re-breathing bag, and monitoring exhaled carbon dioxide. Squeezing the re-breathing bag to confirm intubation may result in regurgitation and is not recommended (Riebold, 1996). If an animal is regurgitating but the endotracheal tube is in the esophagus, then the cuff can be quickly inflated to prevent ingesta from entering the pharyngeal area (Riebold, 1996). Small gazelle species may be inadvertently intubated into a mainstem bronchus. Auscultation of the thorax bilaterally during intermittent positive pressure ventilation should normally reveal lung sounds. If normal sound is only heard on one side, a mainstem bronchus, usually the right, has been intubated and the tube should be backed out (Steffey, 1986). Nasal oxygen should be provided in all species even during short procedures because potent opioids and a2-agonists can cause hypoxemia. There may be difficulty intubating goitered gazelles due to thyroid cartilage impingement on the larynx (Foster, 1999).

Small animal anesthetic machines and ventilators are adequate for maintaining anesthesia in gazelle species. Ruminants typically have higher respiratory rates and smaller tidal volumes under general anesthesia (Riebold, 1996). Therefore, gazelles may require higher vaporizer settings to maintain adequate anesthesia than other species of similar size (Riebold, 1996).

Local or regional anesthetic techniques can be used in gazelles, as they may help provide long-lasting analgesia with the need for less frequent handling. Techniques described for domestic goats and sheep could be used. These techniques are generally underutilized in zoo and wildlife species likely owing to the experience and comfort level of zoo and wildlife veterinarians.

The administration of analgesics can be challenging in gazelle species. Long-acting analgesic techniques or those administered orally are ideal. Oral aspirin at 100 mg/kg per day, or phenylbutazone at 10 to 20 mg/kg per day could be used for short periods of time. If animals can be easily restrained, then administration of drugs on a daily basis by injection could be used, or remote darting systems can be used in some situations. Fentanyl patches may be used for prolonged analgesia but the onset of analgesia may be delayed for 24 hours. In sheep, transdermal fentanyl provided better post-operative analgesia than oral phenylbutazone (Dowd, 1997).

SUPPORT

Non-intubated gazelles should be placed in a sternal position or right lateral recumbency when possible to prevent regurgitation. Often a blindfold is placed over the gazelle's eyes to decrease sensory awareness or excitement. When laterally recumbent for procedures the neck should be supported and the head pointed down to allow saliva and regurgitated material away from the pharynx. After induction gazelles are handled by the horns with the head up and the nose down to prevent aspiration. If the animal is being maintained for surgery, then it should be placed on surgical table with at least 2 inches of padding. Ophthalmic ointment should be applied to eyes to prevent corneal damage.

Intravenous access in gazelle species is typically straightforward. Veins that are easily accessible for catheterizations are the jugular, lateral saphenous, and the cephalic (Figure 55.1). Intravenous fluids or crystalloid solutions are typically given as a supportive measure for prolonged procedures or during surgery. Jugular veins typically can be catheterized with 18-gauge catheters and the lateral saphenous vein is



Figure 55.1. Jugular venipuncture in a Grant's gazelle (Gazella granti). (Courtesy of Dr. Andrea Capobianco Dondona, Oklahoma City Zoo.)

often catheterized with 20- to 22-gauge catheters. If intravenous access is necessary post-immobilization, the jugular vein should be used. Cephalic and saphenous catheters can be difficult to maintain during surgical procedures and after recovery.

Monitoring anesthetic depth can be challenging but should incorporate physical exam findings and cardiopulmonary monitoring. Rotation of the globe of the eye is not an accurate measure of anesthetic depth in gazelles as has been seen in domestic cattle (Riebold, 1996).

Blood pressure can be monitored indirectly with oscillometric measurements from cuffs placed on the limbs. Direct blood pressure can be monitored from auricular or common digital arteries (Figure 55.2).

Placement and flushing of arterial catheters must be done carefully. In one study, a gazelle that died postimmobilization had arterial catheter emboli flushed through the catheter (Schumacher, 1997). Blood pressure can be maintained through lightening of anesthesia, administration of IV fluids, and the use of drugs with positive inotropic, chronotropic, or vasoconstricting effects. These drugs include dobutamine, dopamine, ephedrine, or phenylephrine.

Normal heart rates are 80 to 120 bpm and respiratory rates should be between 20 and 40 bpm. Mean arterial blood pressure should be maintained between 70 and 110 mmHg. Electrocardiography can be used to monitor the cardiac rate and to monitor for any cardiac arrhythmias. End-tidal CO₂ levels and blood gas measurements should also be monitored. With today's portable equipment these monitoring devices are affordable and easy to use in a zoological medicine setting. Pulse oximetry units are very easy to use and portable, making them a sole monitor in many zoo practices. However, pulse oximetry does not replace blood gas measurements for assessing the degree of hypoxemia (Schumacher, 1997). An animal that is being maintained on nasal oxygen



Figure 55.2. Palpation of dorsal common digital artery in an anesthetized Speke's gazelle to prepare for arterial catheterization (Gazella spekei).

may have a normal pulse oximetry reading (greater than 90%) even if hypoventilating. Pulse oximetry estimates the oxygen saturation of hemoglobin; but, when administering high partial pressures of oxygen (nasal oxygen), normal saturation may be maintained even in animals that are not adequately ventilating. If pulse oximetry is the only monitor, then the veterinarian may not be aware of potential impending hypoxic events. Consequently, the adequacy of ventilation should also be measured during prolonged immobilizations through the use of capnography and blood gas measurements. The availability of hand-held blood gas analyzers make blood gas monitoring easier in field situations.

RECOVERY

Gazelles should be recovered in quiet, darkened stalls or barns. Prior to recovery, gazelles may have pieces of garden hose placed over their horns to prevent traumatic injuries or intraspecies aggression during confinement. If the animal has been intubated, the oral cavity should be examined for regurgitated material and the mouth may be swabbed clean. Also, the endotracheal tube can be removed with the cuff partially inflated to help clear the pharyngeal area. A recovering gazelle is usually placed in sternal recumbency with one handler holding the head up with the nose down to prevent aspiration. The gazelle's hind end should be placed near the stall door so that upon recovery it can run away from the handler. The handler can also go out the door quickly to help prevent further excitement upon recovery. Potent opioids are antagonized with naltrexone hydrochloride IV or IM. α_2 -Agonists are antagonized with tolazoline IM or atipamezole IM.

Tranquilizers may be necessary if the animal is being recovered in a new environment or isolated. Agents such as haloperidol, are given before recovery to minimize post-recovery excitement and stress, and are often used in gazelles confined post-immobilization. Haloperidol lactate is a butyrophenone tranquilizer that causes calming and adaptation to a new environment. Haloperidol is typically given at 0.1 to 0.3 mg/kg IM. The onset of action of haloperidol usually occurs within 10 minutes of injection, and effects typically last 18 to 24 hours. This drug is very effective at calming gazelles and preventing self-trauma. The decanoate ester is an oil-based formulation that is much longer acting. This formulation is not commonly used because of the possibility of the extrapyramidal effect of prolonged anorexia. Other long-acting tranquilizers are zuclopenthixol acetate or perphenazine enanthate.

Zuclopenthixol's effects occur within 1 hour and tranquilization may last 3 to 4 days (McKenzie, 1993). Perphenazine effects may not be noted for 12 to 18 hours initially, and may last for 7 days (McKenzie, 1993). The long-acting tranquilizer pipotiazine may have an onset of sedation of 2 to 3 days that may last for greater than

21 days. Zuclopenthixol, perphenazine, and pipotiazine are not currently available in the United States, but formulations are being developed for their use in zoo and wildlife species.

COMPLICATIONS

Exertional myopathy has been associated with the use of etorphine combinations as well as prolonged pacing activity following re-narcotization events (Wallace, 1987; Snyder, 1992; Molnar, 2002). Exertional myopathy can cause acute renal failure resulting from myoglo-bin-related toxic effects on the renal tubules. Exertional myopathy may also result in life-threatening acid-base disturbances and potassium derangements. A ruptured bladder contributed to post-immobilization mortality in a Dama gazelle (Wallace, 1987). This may have resulted from trauma during induction or recovery. Aspiration pneumonia from regurgitated ingesta is a potential problem in anesthetized ruminants.

Hypoxemia often occurs with the use of potent opioids and should be treated with intubation and ventilation. If the animal is not intubated, then nasal oxygen is recommended.

Hypothermia or hyperthermia can result from immobilization and standard treatments have been reported elsewhere.

Renarcotization is a phenomenon in which animals immobilized with potent opioids, particularly carfentanil citrate, exhibit sedation hours after being antagonized. The mechanism by which renarcotization occurs is unknown. Carfentanil citrate has a very long plasma life unless antagonized with naltrexone, but the plasma levels of carfentanil are not consistent with the levels of sedation seen. Therefore, other mechanisms may be responsible in addition to the lingering levels of carfentanil, such as the release of carfentanil from body depots or the underdosing of antagonists (Mutlow, 2004). Studies have shown that animals given lower doses of antagonist re-narcotize, whereas animals given higher doses do not (Haigh, 1995; Miller, 1996). The magnitude and duration of opioid reversal can be dose dependent, but the route of administration has no effect on the antagonism of carfentanil (Mutlow, 2004). Also, certain species are more likely to re-narcotize, which may be a reflection of species differences in opioid receptor affinity for carfentanil or antagonist chosen (Mutlow, 2004). It has been suggested that naltrexone is more effective at preventing renarcotization than nalmefene in Addra gazelles (Gazella dama ruficollis) (Allen, 1996).

Xylazine can have an oxytocin-like effect on the pregnant uterus (Jansen, 1984). The use of detomidine or medetomidine may be preferable in pregnant gazelles. α_2 -Adrenergic agonists as well as opioids can impair gastrointestinal motility. This could lead to tympany and post-anesthetic ileus. α_2 -Adrenergic adrenergic agonists

should be reversed in gazelles with tolazoline or atipamezole (van Miert, 1994). Yohimbine may reverse α agonist effects, but it is less effective in ruminants than tolazoline (Hsu, 1987; Hikasa, 1988). Tolazoline may also bind α_1 -receptors, which could improve ruminalreticular function post-immobilization, and has been shown to more completely restore ruminal-reticular function after the use of α_2 -agonists when compared with yohimbine (Hikasa, 1988). Atipamezole is more effective at reversing central nervous system receptors in sheep, but can cause minor side effects (Hartsfield, 1998; Carroll, 2005). Sudden death can occur in ruminants following reversal of α_2 -adrenergic agonists (Hsu, 1987). The sudden vasodilatory effects of α antagonist drugs may be the reason for the deaths. These vasodilatory effects are less likely to occur when antagonists are administered IM rather than IV.

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56

Wild Sheep and Goats

Nigel Caulkett and Jerry C. Haigh

INTRODUCTION

Capture of wild sheep and goats can be challenging. These animals frequently live in mountainous terrain, and are predisposed to stress-related complications such as hyperthermia and capture myopathy. Wild sheep are frequently captured by physical methods, and manually restrained for short procedures. Remote drug delivery and chemical restraint can be an option if it is carefully planned. Chemical restraint may be more suited for capture of small numbers of animals. Captive sheep and goats may require anesthesia for a variety of reasons. This chapter discusses physical capture methods and current anesthetic techniques for wild sheep and goats.

PHYSICAL CAPTURE VS. CHEMICAL RESTRAINT

In the 1980s several excellent studies critically evaluated capture methods in bighorn sheep (Ovis canadensis) (Kock et al., 1987a,b,c). This body of work evaluated a variety of outcomes to determine the safest capture method for this species.

The studies evaluated three methods of physical capture: drop net, drive net, and net gunning. It also evaluated chemical capture with narcotic-xylazine combinations. The studies compared capture outcome, biological, biochemical, and hematological parameters and long-term survival (Kock et al., 1987a,b,c).

Capture outcome was evaluated by categorizing the animals as normal, stress-induced compromise, and mortality from capture myopathy or trauma. Compromised animals were defined as having one or more of the following signs: body temperature greater than 42.4°C, prolonged pursuit, excessive struggling, shock, or any other signs of physical compromise.

It was determined that net-gunning resulted in the lowest combined mortality rate at less than 2%, drop netting had 3% mortality, and drive netting resulted

in a 4% mortality rate. Chemical immobilization was associated with the highest mortality at 8%. Chemical immobilization was also associated with the greatest number of compromised animals at 19%, drop netting resulted in 15% compromised animals, and drive netting resulted in 16%. Net-gunned animals demonstrated the lowest incidence of compromise at 11% (Kock et al., 1987a). These studies clearly demonstrated that physical restraint was the preferable method for short procedures. For a complete description of these physical capture techniques, please refer to Chapter 12.

CHEMICAL RESTRAINT AND ANESTHESIA

Preanesthetic Concerns

Like all other ungulates, sheep and goats are prone to ruminal tympany and regurgitation during anesthesia. It is prudent to fast captive animals for 24 hours prior to anesthesia. Maintenance in sternal recumbency may help to prevent the onset of ruminal tympany.

Wild sheep and goats often inhabit mountainous terrain. Capture work in this type of terrain must be carefully planned to avoid trauma to the animal during induction of anesthesia. Bighorn sheep are very prone to capture myopathy (Kock et al., 1987c). Capture events must be carefully planned to avoid prolonged chase times in an effort to prevent capture myopathy.

Monitoring and Supportive Care

Sheep and goats are prone to hypoxemia during anesthesia, particularly if α_2 -agonists have been used as part of the anesthetic protocol (Jalanka, 1989; Caulkett et al., 1994; Shury and Caulkett, 2006). Hypoxemia may be less severe if the animal is maintained in sternal recumbency (Caulkett et al., 1996). Oxygenation should always be monitored in anesthetized sheep. Pulse oximetry or arterial blood gas analysis should be used to monitor oxygenation. Oxygen should be available during anesthetic procedures to offset hypoxemia (Figure 56.1).



Figure 56.1. Monitoring oxygen in a bighorn sheep with a pulse oximeter. (Photograph courtesy of Todd Shury.)

Hyperthermia is another potential complication that may be encountered during capture and anesthesia. Hyperthermia has been linked with stress-related complications and capture myopathy (Kock et al., 1987c). It is best to minimize the risk of hyperthermia by limiting pursuit times and planning capture events for cooler seasons when possible. Body temperature should be closely monitored during anesthesia. Body temperature in excess of 41°C should be treated by actively cooling the animal with water or snow. Antagonism of α_2 -agonists should also be considered in emergent situations.

It is difficult to prevent ruminal tympany or regurgitation in free-ranging animals. Maintenance in sternal recumbency may help to prevent or treat ruminal tympany. A rumen tube should be carried to treat serious cases of ruminal tympany. Often it is most advisable to complete the procedure and antagonize α_2 -agonists ruminal tympany typically resolves following administration of an α_2 -antagonist.

Blood pressure monitoring should be considered if the animal is to be maintained with volatile anesthesia. Indirect blood pressure monitors can be used to monitor trends in blood pressure. We typically place the blood pressure cuff midway between the carpus and fetlock joint (Figure 56.2).

Venous access is not difficult in sheep and goats. The cephalic vein, lateral saphenous vein, and jugular vein can all be easily accessed. The auricular artery can be cannulated for direct blood pressure monitoring or to facilitate sampling for arterial blood gas analysis.



Figure 56.2. Indirect blood pressure monitoring in an anesthetized Stone's sheep.

Arterial blood samples may also be obtained from the femoral artery.

Intubation is recommended during volatile anesthesia; it is not difficult in most sheep and goat species. The animal should be maintained in sternal recumbency with the head and neck extended toward the sky. The mouth is opened wide and gentle traction is placed on the tongue. A long flat-bladed laryngoscope is placed into the oral cavity. The tip of the laryngoscope is placed at the base of the epiglottis. The epiglottis is moved ventrally to reveal the glottis. A stylet should be placed inside the endotracheal tube to reduce the curvature of the tube. The tube is placed into the glottis and advanced into the trachea. Typically the tube should not be fully deflated on extubation, as this will help to prevent any rumen contents from entering the trachea if regurgitation has occurred.

Free-ranging animals should be blindfolded to decrease stimulation during light anesthesia or physical restraint. It is important to take care around the legs of lightly anesthetized animals as they may kick. The animal should be placed on a soft surface to avoid pressure points and they should be supported in sternal recumbency for recovery following anesthesia.

Drug Delivery

Helicopter darting and free-range stalking of animals are the major methods used to facilitate drug delivery in wild sheep and goats. Helicopter darting has been associated with increased mortality in bighorn sheep and mountain goats (Kock et al., 1987a; Jessup, 1999). Freerange stalking and ground based drug delivery can also be used to facilitate drug delivery (Festa-Bianchet and Jorgenson, 1985; Merwin et al., 2000; Shurey and Caulkett, 2006). This method can be time consuming and may be best suited to capture of human habituated



Figure 56.3. Ground stalking bighorn sheep in the Canadian rocky mountains. (Photograph courtesy of Todd Shury.)

animals. Ground-based stalking tends to be associated with fewer stress-related complications compared with helicopter darting (Figure 56.3).

Pharmacological Considerations for Anesthesia of Wild Sheep and Goats

Drug Combinations for Remote Delivery Many different drug combinations have been used to facilitate capture of wild sheep and goats. All of these combinations have advantages and disadvantages. In this chapter individual combinations are discussed by species. The chapter focuses on currently used combinations. There are some general principles that are worthy of discussion. α_2 -Agonist-dissociative anesthetic combinations may be associated with less excitement during the induction period, compared with narcotic-based protocols. This may decrease the risk of losing track of a darted animal because of excitement during the induction period. The administration of α_2 -agonists tends to be associated with hypoxemia. Supplemental oxygen should be carried to offset hypoxemia encountered during immobilization. As a general rule yohimbine may not be an effective antagonist for α_2 -agonists in bighorn sheep (Jessup, 1999). Idazoxan has been recommended, but it is difficult to source. We have had good results with atipamezole in a variety of sheep species immobilized with xylazine and medetomidine-based protocols. An appropriate choice of immobilizing drugs should be based on current literature, experience with the drugs, and drug availability.

Volatile Anesthesia

Volatile anesthesia may be used to facilitate maintenance of anesthesia for surgery, imaging, or prolonged procedures. We typically use isoflurane or sevoflurane for maintenance of anesthesia. The sheep or goat is induced to anesthesia with xylazine-telazol or medetomidine-ketamine. Once the animal is recumbent its depth of anesthesia is assessed. If airway protective reflexes are intact either diazepam-ketamine or propofol is administered intravenously to obtund airway protective reflexes and facilitate intubation. We typically use a dose of 0.1 mg/kg of diazepam, combined with 2 mg/kg of ketamine, administered to effect. Propofol is administered at 1 to 2 mg/kg. Commonly encountered side effects of volatile anesthesia are respiratory depression and hypotension. Respiratory depression is typically treated with intermittent positive pressure ventilation and hypotension often responds to a lightening of the anesthetic plane or fluid therapy. Body temperature should be closely monitored, as hypothermia may be encountered, particularly in smaller animals.

Once the procedure is complete it is advisable to antagonize residual α_2 -agonist drugs, otherwise prolonged recoveries may be encountered.

Species-Specific Considerations

Bighorn Sheep (*Ovis canadensis canadensis*) and Dall or Stone's Sheep (*Ovis dalli*) Narcotic-based anesthesia with carfentanil-xylazine or etorphine-xylazine has been used for helicopter-based capture of bighorn sheep. Etorphine has been used at a dose of 3.5 mg, combined with 50 mg of xylazine. Carfentanil has been used at 0.044 mg/kg in combination with 0.2 mg/kg of xylazine (Jessup, 1999). Both of these combinations can be used to successfully capture sheep. Complications tend to occur with partial dosing or trauma during induction. This may reflect the method of capture (helicopter darting) more than an actual drug effect.

Xylazine-ketamine combinations have been used for capture of bighorns (Festa Bianchet and Jorgenson, 1985). Xylazine-ketamine solutions must be delivered in relatively high volumes; therefore, this mixture has been largely replaced by xylazine-telazol. Xylazine-telazol has been used to effectively capture human habituated bighorn sheep. It has been advocated at a dose of 4.2 mg/kg of telazol combined with 0.5 mg/kg of xylazine (Merwin et al., 2000). A major drawback of this mixture is that recoveries tend to be prolonged following antagonism of the xylazine; this is probably the result of residual telazol. To address this concern we have recently started using a mixture of xylazine, telazol, and hydromorphone (Shurey and Caulkett, 2006). This mixture is administered at a dose of 1.64 mg/kg of telazol combined with 1.1 mg/kg of xylazine and 0.22 mg/kg of hydromorphone. The mixture proved to be suitable for capture of human-habituated sheep. Recovery was relatively rapid (10.3 minutes) following the administration of 0.11 mg/kg of atipamezole and 0.18 mg/kg of naltrexone.

We have also used 0.06 to 0.08 mg/kg of medetomidine, combined with 2 mg/kg of ketamine to induce

anesthesia in captive bighorn sheep. This combination is readily reversed with atipamezole at three times the medetomidine dose.

In our experience Dall and Stone's sheep are very similar to bighorn sheep. We have used 1 mg/kg of xylazine combined with 2 mg/kg of telazol for induction prior to administration of volatile anesthetics in captive Stone's sheep. We have also used 0.06 to 0.08 mg/kg of medetomidine, combined with 2 mg/kg of ketamine in captive Dall and Stone's sheep.

Mountain Goat (*Oreamnos americanus*) Free-ranging mountain goats have typically been anesthetized with potent narcotics. Carfentanil has been advocated, as the sole agent, at a dose of 0.035 mg/kg (Jessup, 1999). Etorphine has also been used at a dose of 4 to 5 mg per animal (Jessup, 1999). We have anesthetized captive mountain goats with 0.06 to 0.08 mg/kg of medetomidine, combined with 2 mg/kg ketamine. This dose produces light anesthesia for restraint or as a premedication for general anesthesia. The medetomidine is readily antagonized with atipamezole administered at three times the medetomidine dose.

Markhor (*Capra falconeri megaceros*) A detailed study exists that compares the efficacy and safety of medeto-midine-ketamine and etorphine-acepromazine in captive Markhors (Jalanka, 1989). This study compared a mean dose of 63 μ g/kg of medetomidine, combined with 1.6 mg/kg of ketamine against 56 μ g/kg of etorphine, combined with 0.25 mg/kg of acepromazine. Both of these combinations were readily reversible. Atipamezole was used at a mean dose of 282 μ g/kg, and diprenorphine was administered at a dose of 76 μ g/kg.

Both combinations induced moderate hypoxemia. Medetomidine-ketamine induced slightly more respiratory depression evidenced by a significantly greater $PaCO_2$, compared with etorphine-acepromazine. Medetomidine-ketamine produced better myorelaxation and a more complete immobilization than etorphine-acepromazine (Jalanka, 1989).

Medetomidine-ketamine has become a commonly recommended combination for anesthesia of sheep and goats.

Chamois (*Rupricapra rupicapra*), Alpine Ibex (*Capra ibex*), Barbary Sheep (*Ammotragus Iervia*), Himalayan tahr (*Hemitragus jemlahicus*), Mouflon (*Ovis musimon*) All of these sheep and goat species can be effectively immobilized with medetomidine-ketamine. The following doses have been used in captive animals (Jalanka and Roeken, 1990). Chamois: 70 to 100 μg/kg of medetomidine combined with 1.5 to 2 mg/kg of ketamine. Alpine ibex: 80 to 140 μg/kg of medetomidine combined with 1.5 mg/kg of ketamine. Barbary sheep: 100 to 140 μg/kg of medetomidine combined with 1.5 mg/kg of ketamine. Himalayan tahr: 80 to 100 μg/kg of

medetomidine combined with 1.5 mg/kg ok ketamine. Mouflon: $125 \mu g/kg$ of medetomidine combined with 2.5 mg/kg of ketamine.

All of the preceding doses were used in captive animals. It may be necessary to increase the dose in free-ranging animals. It is important to allow adequate time for induction with medetomidine-based protocols, as animals may rouse and flee if they are approached too early. Typically the animal can be approached approximately 5 minutes post-induction.

Muskox (Ovibos moschatus) Muskox anesthesia can be somewhat more challenging than anesthesia of the smaller sheep and goat species. Their head is relatively large and they have a small oral cavity, which can make intubation a challenge. We typically use a mouth gag to open the mouth, and use a long flat laryngoscope blade to visualize the glottis. It is important to induce good muscle relaxation to facilitate intubation. We have used 0.05 to 0.1 mg/kg of diazepam or 5% guaifenesin, given to effect, to induce muscle relaxation. Manual intubation may be attempted in large muskox. The endotracheal tube is guided into the trachea manually by placing a hand dorsally over the end of the tube and advancing the hand into the pharynx. Once the operator's hand is in the pharynx the epiglottis is reflected ventrally and the tube is advanced into the trachea (Figure 56.4).

Free-ranging adult muskox have been immobilized with 2 mg of etorphine, combined with 30 mg of xylazine and 200 IU of hyaluronidase (Clausen et al., 1984).

We have used 50 to $60 \,\mu\text{g/kg}$ of medetomidine, combined with 1.5 mg/kg of ketamine for short-term anesthesia of muskox. We have also used 0.5 to 1 mg/kg of



Figure 56.4. Intubation of Muskox can be difficult. It may be attempted by palpation in large animals. A long laryngoscope blade is required in smaller animals. (Photograph courtesy of Jessica Paterson.)

xylazine alone, or combined with 1 to 2 mg/kg of ketamine for deep sedation of captive muskox. These animals were relatively tame and human habituated, and these doses should not be extrapolated to wild muskox.

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57

Non-domestic Cattle

Thomas G. Curro

INTRODUCTION

The family Bovidae consists of nine subfamilies, one of which is the Bovinae. This subfamily consists of the oxen and antelope. The wild oxen are the focus of this chapter. These animals live in habitats as varied as dense forest, open grassland, and montane; and are generally gregarious in nature. Species considered include: gaur (Bos frontalis), banteng (Bos javanicus), African buffalo (Syncerus caffer), forest buffalo (Syncerus caffer nanus), yak (Bos grunniens), anoa (Bubalus depressicornis), and ankole or watusi (Bos primigenius f. taurus).

Adults of the wild oxen species range in body weight from 150 to 1,000 kg (Table 57.1).

The anatomy and physiology of these bovids are quite similar to that of domestic cattle. Therefore, there are no special anesthetic considerations regarding anatomy and physiology, other than those discussed in sections that follow, related to these species that would not be considered when anesthetizing domestic cattle. In particular, Asian buffalo (*Bubalus bubalis*), in their native countries, are treated anesthetically in a similar manner as domesticated cattle.

ANALGESIA

In any situation in which an animal is perceived to be, or expected to be, experiencing pain, analgesics should be considered for administration. Analgesic agents include opioids, α_2 -adrenergic agents, and nonsteroidal anti-inflammatory drugs (NSAIDs). Opioids and α_2 -agents, commonly used for sedation and general anesthesia provide analgesia during these periods. Detomidine analgesia in domestic cattle has a duration of action up to 2.5 hours. Detomidine administered at 0.04 mg/kg intramuscularly (IM) has demonstrated analgesia comparable with epidurally administered detomidine in domestic cattle (Prado 1999). Because of the potential sedative effects, opioids and α_2 -agents are

less likely to be employed for analgesia outside of anesthetic events, unless the animal will be confined to a stall or boma. Sedation in an unconfined situation may lead to trauma by conspecifics, if in a herd, or environmental hazards.

NSAIDs offer the ability to produce analgesia without the complication of sedation. There are no recent publications demonstrating the effectiveness of NSAIDs in exotic cattle. However, studies in domestic calves undergoing horn disbudding, and domestic bulls undergoing castration, have shown that administration of ketoprofen at 3.0 mg/kg IV produces analgesia (Faulkner, 2000; Ting, 2003). Phenylbutazone may also be used as an analgesic in cattle orally at 10 mg/kg every 48 hours. Meloxicam at 0.5 mg/kg has demonstrated non-immunosuppressive anti-inflammatory benefits in cattle with respiratory disease (Bednarek, 2005; Friton, 2005). Therefore, meloxicam may be an effective analgesic for inflammation-related pain, although there are no published reports of this being studied in cattle.

PRE-ANESTHETIC CONSIDERATIONS

Because of the large size and potentially aggressive temperament of exotic cattle, measures should be taken to perform restraint and anesthetic events safely for the animals and the staff involved. All participants should be briefed on how the event will take place, and what contingencies may go into effect if the stated plan does not go as expected.

The environment should be considered. Ideally, the animal should be confined to the smallest and quietest enclosure that will allow manipulation of the animal once it is anesthetized. The ability to dim the lights is also an asset. If the animal will be lying on concrete or firm surfaces for an extended period of time, protective padding should be used.

In herd or open field situations, in which there is less control of the environment, efforts should be made to

Table 57.1. Estimated average body weights of large non-domestic bovids.

Species	Body Weight (kg) ^a
African buffalo	600-900
Ankole, Watusi	400-725
Anoa	150-300
Asian buffalo	800-1000
Banteng	400-900
Forest buffalo	200-300
Gaur	650-1000
Yak	330-1000

^aFemales are in the lower range, whereas males are in the upper range of the body weight estimates.

eliminate the opportunity for the animal to enter water or encounter terrain changes, such as drop-offs or cliffs. This may require recruitment of many staff and vehicles to corral and maintain the animal in a specific location.

The animal should be fasted whenever possible because of the large volume of rumen contents in adult bovids, and the potential for passive regurgitation of the contents during periods of recumbent anesthesia. Food should be withheld for 18 to 36 hours, whereas water should be withheld for 8 to 12 hours. Fasting aids in decreasing the amount of rumen contents and its potential for regurgitation. Fasting also decreases the chance for development of rumen tympany. Decreasing the chance of passive regurgitation decreases the chance for aspiration of the contents into the respiratory system, preventing the potential occurrence of aspiration pneumonia. In situations in which an animal cannot be adequately fasted, as in open field conditions, efforts should be made to approach it as soon as it can be safely manipulated.

Placing the animal in sternal recumbency for the duration of the procedure may be effective in decreasing the chance of rumen regurgitation. If sternal recumbency cannot be maintained, measures should be taken to prevent aspiration in the event of regurgitation. If there is a slope to the environment, position the animal so the head is at the downward-most direction of the slope. If there is no slope, then prop the head and neck such that the opening of the oral cavity is lower than the pharynx. Either of these positions allows contents to flow from the oral cavity, decreasing the chance of aspiration. The only way to significantly decrease the chance of aspiration of regurgitated rumen contents is to endotracheally intubate the animal, as described, as early in the anesthetic event as possible.

PHYSICAL RESTRAINT

For minor procedures, such as tuberculosis testing, blood sampling, rectal and vaginal examinations, and medication administration, it may be possible to use physical restraint devices. Common devises include box

chutes, a head gate stanchion incorporated into a squeeze chute, and a drop chute. These devices may have limitations, mainly relating to body and horn size of the animal.

To use these devices, a corral and walkway system must be available that allows directing of the animal into the chute. Allowing the animal to pass through the corral and into the chute system in short stages may prevent the animal from charging with enough force to produce head trauma. This may be accomplished with intermittent gates or turns in the walkway. Sedation with xylazine (0.15–0.20 mg/kg) prior to exposing animals to the chute may increase their compliance.

Commercially available restraint devices include manual squeeze chutes (Heavy Duty Squeeze Chute, Powder River Livestock Equipment, Provo, UT) (Read, 1989), drop-floor chutes (The Tamer, Fauna Research, Red Hook, NY), and hydraulic squeeze chutes (Hydraulic Tamer, Fauna Research) (Blumer, 1991; Citino, 2003). Once an animal is in a drop chute, the floor can be lowered, allowing the animal to rest in the wedge of the chute. As they no longer have supportive footing, they tend to stop struggling, which allows procedures to be performed.

Restraint devices should have removal panels at strategic places to allow access to the animal for procedures. Any physical restraint device must have a quick-release mechanism in the event the animal has problems. These situations might include getting the head or legs caught in an abnormal position, collapsing within the chute, or being too active to the point of producing self-trauma.

SEDATION/AGENTS

Short- and long-acting sedatives are available for exotic bovids. The most commonly used short sedatives in large cattle are the α_2 -adrenergic agents, xylazine, detomidine, and medetomidine (Short, 1992). In cattle with a relatively calm temperament, the α_2 -agents produce a calming state. However, these agents can be over-ridden by an animal that is easily excited. Standing sedation in domestic cattle has been attained with intravenous (IV) xylazine (0.02 mg/kg) or detomidine (0.01 mg/kg), with an extended duration of action when either is combined with butorphanol (0.05 mg/kg) (Lin, 2003). African buffalo may be sedated or immobilized with xylazine at dosages of 0.05 to 0.15 mg/kg or 0.2 to 0.4 mg/kg, respectively (Fowler, 1995). IM detomidine (0.04 mg/kg) induces standing sedation in domestic cattle. Sedation with detomidine IM at 0.03 to 0.08 mg/kg has been attained in domestic cattle within 1 to 10 minutes of administration. Detomidine has been used to sedate domestic calves at dosages of 0.01 mg/kg for light sedation, and 0.02 to 0.04 mg/kg for deep sedation (Peshin, 1991). Free-ranging Norwegian cattle have been sedated with xylazine (37–73 mg/kg) or medetomidine

(0.029–0.049 mg/kg) (Arnemo, 1993). Medetomidine (0.07 mg/kg) produces deep sedation in yaks administered IM, whereas detomidine (0.025 mg/kg) produces light sedation (Sharma, 1998, 2001).

Acepromazine, an intermediate-acting phenothiazine tranquilizer, has been used on its own to sedate domestic bovids, but is more frequently used in combination with other anesthetics to immobilize exotic bovids. When used alone at an IM dosage of 0.05 to 0.10 mg/kg, the onset is 10 to 20 minutes with a duration of 4 to 8 hours, and potential residual effects out to 12 hours (Blumer, 1991; Swan, 1993).

Haloperidol is an intermediate-acting butyrophenone tranquilizer, used in a variety of ungulates (Blumer, 1991). It has an onset of 5 to 10 minutes, and a duration of 8 to 18 hours. Azaperone (0.10–0.15 mg/kg) or haloperidol (0.01–0.03 mg/kg) has been used for IM sedation in African buffalo. Haloperidol has been shown to be an effective sedative when given orally to small exotic bovids at 1.0 mg/kg per day.

Benzodiazepine use has been reported in bovids. Midazolam is more commonly combined with another general anesthetic, although it may be used as a sedative in young calves. Although diazepam sedation has been attempted in yak, this may produce violent inductions, falling with unsuccessful attempts to rise, and paddling of the limbs (Kumar, 1999). Therefore, diazepam should not be used alone in the sedation of yak.

Zuclopenthixol acetate, an intermediate long-acting thioxanthene tranquilizer, has been used in African buffalo (1 mg/kg), and various exotic free-ranging and captive ungulates. When administered IM, the onset is 60 minutes, with a duration of 72 to 96 hours (Swan, 1993; Ebedes, 1995; Citino, 2003). Perphenazine enanthate, a long-acting phenothiazine sedative, has been used IM in gaur to reduce stress-induced self-trauma. This sedative has an onset time of 12 to 16 hours, and a duration of action of 72 to 168 hours (Swan, 1993; Blumer, 1991; Ebedes, 1995; Citino, 2003). Pipotiazine palmitate, a very long-acting phenothiazine sedative, has an onset of 48 to 72 hours, with a duration of action up to 30 days with IM dosage ranges from 1.0 to 2.5 mg/kg (Blumer, 1991; Swan, 1993; Ebedes, 1995; Citino, 2003). Zuclopenthixol and perphenazine or pipotiazine may be used concurrently to get the initial effects of zuclopenthixol followed by the longer duration of perphenazine or pipotiazine.

GENERAL ANESTHESIA AND AGENTS

Many general anesthetic techniques and agents have been used on large bovids (Table 57.2). The major drug classes commonly used include opioids, α_2 -adrenoceptor agents, and dissociatives. Techniques and agents vary depending on their regional availability.

The route of most general anesthetics is IM. If the animal is confined to a small stall, a pole syringe can be

used. Commonly, darts are used to administer IM injections. In select situations with young calves, with appropriate physical restraint, mask induction with inhalant anesthetics may be used to induce general anesthesia. Isoflurane and sevoflurane are commonly used for this purpose. An African buffalo calf has been induced with midazolam and ketamine prior to intubation for inhalant maintenance (Stegmann, 2004).

Where opioids are available, they are the most commonly used group of drugs to produce general anesthesia in large bovids. The most commonly used opioids include etorphine and carfentanil. Thiafentanil has been studied in various hoofstock (Janssen, 1991), and may be available on a research basis at this time. Dosages for etorphine range from 0.005 to 0.050 mg/kg, whereas dosages for carfentanil range from 0.005 to 0.015 mg/kg. Dosages for thiafentanil range from 0.007 to 0.018 mg/kg. Induction times are longest for etorphine, shortest with thiafentanil, and intermediate with carfentanil. Thiafentanil may have induction times of 2 to 3 minutes. The addition of hyaluronidase, which increases the rate of absorption of the concurrent opioid, may decrease induction times by as much as 50%. Opioids are routinely used in combination with α_2 -agents (xylazine, detomidine, and medetomidine), as well as the phenothiazine, acetylpromazine. This decreases the amount of opioid needed to produce a given effect. Combinations may also improve muscle relaxation. The α_2 -agents or phenothiazines may be given 15 to 20 minutes prior to the opioid, or they may be combined with the opioid for a single injection. A combination of thiafentanil, medetomidine, and ketamine has been used in field conditions producing rapid onset and good muscle relaxation. African Buffalo are routinely immobilized with a combination of etorphine (0.01 mg/kg) and azaperone (0.15–0.2 mg/kg). Gaur may be effectively immobilized with xylazine (0.08-0.10 mg/kg) and carfentanil (0.005-0.010 mg/kg) (Armstrong, 1989; Wilson, 1993). In the event that the initial opioid protocol does not produce adequate anesthesia, administering another intramuscular dose of the initial drugs at half the initial dosage can be given.

If initial effects are insufficient for safe handling, but allow for intravenous access, supplementation with ketamine (0.10–1.0 mg/kg), α_2 -agents (0.05–0.20 times the initial dose), glycerol guaiacolate (guaifenesin 5%) (0.5–2.0 mg/kg drip to effect), alone or in combinations, may be administered to attain an immobilizing level of anesthesia. Propofol (0.20–1.0 mg/kg) may also be used IV for this purpose, as has been reported in yak and European bison (Jalanka, 1992). Glycerol guaiacolate has been shown to improve muscle relaxation on immobilization with opioids (Janssen, 1984).

Because of their extreme potency (in relation to morphine), etorphine, carfentanil, and thiafentanil are classified as ultra-potent opioids. Appropriate precautions should be taken when using these drugs, to prevent

Table 57.2. Recommended anesthetic agents and protocols for large non-domestic bovids.

Species	Anesthetic Agent(s) (mg/kg)	Antagonist(s) (mg/kg)	Desired Effect
African buffalo	Xylazine: 0.05-0.15		Sedation
	Xylazine: 0.20-0.40		Immobilization
	Xylazine: 0.10 Etorphine: 0.012	Diprenorphine: 0.024	Immobilization
	Xylazine: 0.08–0.18 Acepromazine: 0.02–0.03 Etorphine: 0.005–0.007	Diprenorphine: 0.010-0.014	Immobilization
	Azaperone: 0.15 Etorphine: 0.015	Diprenorphine: 0.030	Immobilization
	Carfentanil: 0.006-0.008	Naltrexone: 0.6-0.8	Immobilization
	Xylazine: 0.028-0.050 Carfentanil: 0.002-0.005	Naltrexone: 0.2–0.5	Immobilization
	Azaperone: 0.06-0.07 Thiafentanil: 0.007-0.014	Naltrexone: 0.07-0.14	Immobilization
Ankole, Watusi	Xylazine: 0.14-0.70 Etorphine: 0.014-0.038	Atipamezole: 0.03 Diprenorphine: 0.028-0.076	Immobilization
	Acepromazine: 0.10–0.14 Etorphine: 0.024–0.034	Diprenorphine: 0.048-0.068	Immobilization
	Detomidine: 0.05–0.08 Butorphanol: 0.08–0.20	Atipamezole: 0.03–0.15 Naltrexone: 0.05–1.0	Sedation
	Detomidine: 0.019-0.029 Carfentanil: 0.006-0.010 Ketamine: 0.30	Atipamezole: 0.10 Naltrexone: 0.6–1.0	Immobilization
	Detomidine: 0.005 Acepromazine: 0.04–0.05 Etorphine: 0.016–0.019 Ketamine: 0.48–0.50	Atipamezole: 0.03 Naltrexone: 1.8	Immobilization
	Detomidine: 0.12 Acepromazine: 0.04 Carfentanil: 0.012 Ketamine: 0.40	Yohimbine: 0.33 Naltrexone: 1.2	Immobilization
Anoa	Xylazine: 1.0 Ketamine: 6.0	Atipamezole: 0.2	Immobilization
	Xylazine: 0.27–0.33 Acepromazine: 0.11–0.12 Etorphine: 0.027–0.033	Diprenorphine: 0.054-0.066	Immobilization
	Xylazine: 0.05-0.25 Carfentanil: 0.01-0.03	Naltrexone: 1.0–3.0	Immobilization
	Medetomidine: 0.025–0.100 Ketamine: 0.05–2.0	Atipamezole: 0.12–0.50	Immobilization
Banteng	Xylazine: 0.03–0.22	Yohimbine: 0.07–0.18	Sedation (o) Immobilization
	Xylazine: 1.5 Xylazine: 0.05–0.09 Acepromazine: 0.06–0.10	Atipamezole: 0.04-0.08	Sedation (q)
	Xylazine: 0.75–1.00 Ketamine: 1.5–2.0	Atipamezole: 0.06–0.08	Immobilization
	Xylazine: 0.056–0.125 Acepromazine: 0.02–0.05 Etorphine: 0.005–0.012	Diprenorphine: 0.010-0.024	Immobilization
	Xylazine: 0.05-0.25 Carfentanil: 0.001-0.008	Naltrexone: 0.1-0.8	Immobilization
	Xylazine: 0.11 Carfentanil: 0.007 Ketamine: 0.15	Naltrexone: 0.7	Immobilization
	Detomidine: 0.059-0.079 Butorphanol: 0.050-0.088	Yohimbine: 0.21–0.22 Naltrexone: 0.84–0.88	Sedation

Table 57.2.(Continued)

Species	Anesthetic Agent(s) (mg/kg)	Antagonist(s) (mg/kg)	Desired Effect
	Detomidine: 0.069–0.104 Butorphanol: 0.071–0.083 Ketamine: 0.69–2.13	Yohimbine: 0.18–0.20 Naltrexone: 0.7–0.9	Immobilization
	Detomidine: 0.009–0.014 Carfentanil: 0.010–0.017 Ketamine: 0.33–2.78	Atipamezole: 0.05 Naltrexone: 1.0–1.7	Immobilization
Forest Buffalo	Xylazine: 0.09-0.33 Etorphine: 0.012-0.050	Atipamezole: 0.027–0.033 Diprenorphine: 0.024–0.10	Immobilization
	Acepromazine: 0.07–0.10 Etorphine: 0.018–0.024	Diprenorphine: 0.036-0.048	Immobilization
	Xylazine: 0.14–0.18 Acepromazine: 0.13–0.14 Etorphine: 0.031–0.036	Diprenorphine: 0.062-0.072	Immobilization
	Xylazine: 0.06–0.13 Carfentanil: 0.011–0.012 Ketamine: 1.55–2.50	Yohimbine: 0.11–0.12 Naltrexone: 1.1–1.2	Immobilization
Gaur	Xylazine: 0.12–0.22 Acepromazine: 0.04–0.09 Etorphine: 0.010–0.022	Diprenorphine: 0.020-0.044	Immobilization
	Xylazine: 0.05-0.25 Carfentanil: 0.01-0.03	Naltrexone: 1.0–3.0 ^a	Immobilization
	Xylazine: 0.125 Carfentanil: 0.005 Ketamine: 0.06–0.09	Naltrexone: 0.5	Immobilization
	Xylazine: 0.05-0.25 Thiafentanil: 0.011-0.018	Naltrexone: 0.11-0.18	Immobilization
Yak	Xylazine: 0.30 Xylazine: 0.6–1.0		Sedation Immobilization
	Xylazine: 0.04 Etorphine: 0.006	Diprenorphine: 0.012	Immobilization
	Xylazine: 0.05–0.20 Acepromazine: 0.025–0.10 Etorphine: 0.006–0.024	Diprenorphine: 0.012-0.048	Immobilization
	Xylazine: 0.40–1.67 Acepromazine: 0.04–0.05 Etorphine: 0.010–0.012 Ketamine: 0.04–1.67	Diprenorphine: 0.020-0.024	Immobilization
	Xylazine: 0.10 Carfentanil: 0.0075	Naltrexone: 0.75	Immobilization
	Medetomidine: 0.10 Ketamine: 3.0	Atipamezole: 0.5	Immobilization

Note: The dosages and protocols presented in this table are a compilation of information from the listed references, personal experience, and personal communication with staff from the following institutions: Denver Zoo, Denver, Colorado, USA; Disney Animal Kingdom, Lake Buena Vista, Florida, USA; Exotic Animal Service, Edinburgh University, Edinburgh, UK; Marwell Preservation Trust, Winchester, UK; Royal Zoological Society of Antwerp, Antwerp, Belgium; Suffolk Wildlife Park, Edinburgh, UK; St. Louis Zoo, St. Louis, Missouri, USA; Whipsnade Wild Animal Park, Bedfordshire, UK; Zoological Society of London, London, UK.

accidental human injection, which may lead to serious complications and death. Personal protective equipment should be used. Minimally, eye protection and impermeable gloves should be worn. Antagonists should be available on site, and should be prepared for injection prior to the preparation of the ultra-potent

opioids. Careful record keeping of the use of opioids is required by governmental drug agencies.

Where opioids are unavailable, combinations of α_2 -agents or benzodiazepines with a dissociative are commonly used (Barnett, 1990). Ketamine is the most commonly used dissociative, although the combination

 $^{^{}a}$ Naltrexone in Gaur is administered 30%–50% IV and 50%–70% IM, which may reduce renarcotization.

of tiletamine and zolazepam (Telazol, Zolatil) has been used. Medetomidine may be combined with a reduced dosage of ketamine, compared with xylazine, allowing for potentially smoother recoveries. Detomidine in combination with Zoletil has been successfully used to immobilize wild banteng (Bradshaw, 2005). Telazol has been studied in Gaur, but the quality of induction and maintenance was poor (Wilson, 1993). A combination of detomidine (0.01 mg/kg), diazepam (0.01 mg/kg), and ketamine (3.0 mg/kg) has been used for heavy sedation in Asian buffalo calves (Pawde, 2000). Again, if after the initial doses are administered an acceptable level of anesthesia is not attained, lesser doses of the agents can be given intravenously or intramuscularly.

In many instances, intramuscular administration of anesthetic agents is the only route available. Barbiturates are uncommonly used agents for general anesthesia in large exotic cattle owing to their need to be administered IV. Likewise, induction of anesthesia with glycerol guaiacolate is used in combination with dissociatives and barbiturates in domestic cattle, but less so in exotic cattle because of the need for IV administration. If venous access is available, these drugs may be used at domestic cattle dosages, and propofol may be used for induction at dosages of 2.0 to 4.0 mg/kg (Jalanka, 1992).

If an anesthetic episode is to be prolonged (greater than 1 hour), consideration should be given to maintaining anesthesia with an inhalant anesthetic, such as halothane, isoflurane, and sevoflurane. Procedures and protocols at this point are similar to those used in domestic cattle.

ENDOTRACHEAL INTUBATION

Endotracheal (ET) intubation may be required for administration of inhalant anesthetics, or to prevent aspiration of regurgitated rumen contents. The most commonly used ET tubes are made of silicone rubber, contain a Murphy eye, and incorporate an inflatable cuff, which allows sealing of the airway. Calves of exotic bovid species may be intubated with direct visualization of the airway, whereas adults will likely need to be intubated by palpation.

Calves should be placed in sternal recumbency, with the head and neck extended so that the nose of the animal is directed upward. While an assistant holds the maxilla and mandible apart, the tongue is extended rostrally and off to one side. A laryngoscope is then inserted on the opposite side of the mouth from the extended tongue, which will allow the operator to visualize the larynx for passage of the ET tube into the trachea.

Adults may be intubated in sternal or lateral recumbency, with the head and neck in an extended position. An appropriately sized oral speculum should be used when intubating adult animals. The ET tube is manually directed through the oral cavity until the epiglottis is

reached. The epiglottis is deviated ventrally, and the ET tube is guided into the trachea.

VASCULAR ACCESS

Vascular access is needed to collect blood samples. Venous access may be required to administer supplemental anesthetics, anesthetic antagonists, medications, emergency drugs, or fluids. Arterial access allows sampling for blood gas analysis, or systemic blood pressure assessment.

Common sites for venous access include the jugular, auricular, and lateral saphenous veins. Arterial access is commonly attained via the caudal auricular artery. The ventral coccygeal artery and vein may also be used for blood sampling.

MONITORING

A permanent record of an anesthetic event should be completed for each animal. This data may then be stored for retrieval in an institution's preferred data base system. Careful monitoring of an animal while anesthetized may alert and/or prevent significant anesthetic-related complications.

To assess the depth of anesthesia, noting the animal's response to its environment is important. At times with the use of opioids, the animal will remain standing, but be relatively unaware of its surroundings. The animal may need to be manually positioned in recumbency. Most of the time, a recumbent position is attained without assistance. Once the animal reaches a light plane of anesthesia, there should be minimal response to tactile stimulus. The globe of the eye rotates ventromedially during this stage. At a deep surgical plane, the globe rotates back to a central position (Reibold, 1982).

Minimally, body temperature, heart rate, and ventilatory rate should be monitored. Rectal temperature measurement is most commonly performed. The normal body temperature should range from 37°C to 39°C (99°F–102°F). If an animal's body temperature rises above 39.5°C (103°F), cooling procedures should be instituted, as described in the following.

Heart rate may be monitored directly by auscultation with a stethoscope, or indirectly with an electrocardiograph (ECG) or an oscillometric systemic blood pressure measuring device. Ventilatory rate is most commonly monitored by direct observation of the animal's thorax and abdomen during breathing excursions.

An ECG leads should be attached in a base-apex configuration. Minimally, the positive lead should be placed on the thorax adjacent to the left elbow, and the negative lead should be placed over the right jugular furrow near the thoracic inlet. In standard ECG terms, the red lead is placed on the thorax, and the white lead is placed over the jugular furrow. If the ECG requires

placement of three leads; the black lead would be placed over the left jugular furrow.

Peripheral pulse rate and quality may be assessed by palpation of the caudal auricular or common digital arteries. In young animals, the facial artery may be palpated, but in adults, this artery is less accessible. A Doppler flow detector may be used to assess pulse rate when placed over an accessible artery. If the artery is accessible distally on a limb, a blood pressure cuff and manometer, in conjunction with the Doppler flow detector, may be used to evaluate systolic blood pressure, indirectly.

Systemic blood pressure may be monitored directly or indirectly. Direct measurement requires arterial access via catheterization. The caudal auricular artery is commonly catheterized for this purpose. Indirect measurement may be performed with a blood pressure cuff placed at the base to the tail. Besides the Doppler system mentioned, various companies now manufacture oscillometric blood pressure machines. Mucous membrane capillary refill time, usually 1 to 2 seconds, gives a cursory determination of tissue perfusion.

Blood gases may be used to monitor the adequacy of ventilation and hemoglobin oxygen saturation, and the acid-base status of the animal during anesthesia. Mucous membrane color will give a cursory determination of oxygenation.

RECOVERY

Once all procedures have been completed, and it is safe to due so, all monitoring devices should be removed from the animal, and all equipment should be removed from the recovery area. If any rope restraints were used, they should also be removed from the animal.

A quick survey of the environment should be done. Any potential hazards should be addressed. This is a factor in field situations in which the landscape may provide uneven terrain or water hazards. If possible, these areas should be barricaded.

If an opioid or α_2 -adrenergic agent is used, the antagonists to these drugs should be administered to speed the recovery from the anesthetic event. Naltrexone is a preferred antagonist for carfentanil. The dose depends on the dose of carfentanil administered. In captive situations, the dosage is 100 mg naltrexone per 1 mg of carfentanil given. In field situations, the dosage is 150 mg of naltrexone per 1 mg of carfentanil, to decrease the chance of renarcotization. Thiafentanil may be antagonized with naltrexone at a dose of 10 mg of naltrexone per mg of thiafentanil.

 α_2 -Adrenergic antagonists include yohimbine for the reversal of xylazine and detomidine, and atipamezole for reversal of medetomidine. Atipamezole may also be used to antagonize xylazine and detomidine.

In situations in which an endotracheal tube was used, it should be withdrawn as soon as the animal

begins to show signs of pharyngeal activity. The endotracheal tube cuff, if inflated appropriately, does not need to be deflated prior to tube removal. This aids in removing any oral secretions that may have accumulated in the trachea distal to the cuff. Of course, removal of the endotracheal tube should be evaluated in light of the safety margin needed for staff to clear away from the animal once it has recovered.

COMPLICATIONS

Because of the potential excitable behavior of these animals, it is not uncommon for them to traumatize themselves, or become hyperthermic during anesthetic induction. This is especially evident in animals in field situations in which they may run great distances during the immobilization process from darting to recumbency. High environmental temperature and humidity, and prolonged, severe muscle exertion may precipitate a hyperthermic state. A body temperature exceeding 39.5°C (103°F) should be considered a hyperthermic state. A source of cold water should be available for treatment via topical application and rectal enemas. Treatment for capture myopathy should also be considered.

If excessive rumen gas production leads to tympany, a stomach tube should be inserted in an attempt to remove the gas. This is an infrequent problem in fasted animals, but may be of greater concern in non-fasted animals.

It is not uncommon for certain bovids, especially gaur, to reach a state of renarcotization 12 to 24 hours after naltrexone antagonism of carfentanil anesthesia. If an animal begins to demonstrate signs of agitation, mild excitement, forward pacing, a high-stepping gate, or any other signs one would expect to see as the early signs of opioid narcotization, renarcotization should be considered. Intramuscular administration of a 50% dose of the initial antagonist dose should be given. Signs of renarcotization should subside within 5 to 15 minutes.

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Bison

Nigel Caulkett and Jerry C. Haigh

INTRODUCTION

Two subspecies of bison can be found in North America. The plains bison (*Bison bison bison*) is most commonly encountered in free ranging and captive herds. The wood bison (*Bison bison athabascae*) is confined to a few free-ranging herds in northern Canada, and some captive animals. Response to anesthesia is similar in both subspecies and this discussion applies equally to both. There are wild populations of the European bison (*Bison bonasus*) in Poland, Russia, Belarus, Ukraine, and the western Caucasus. The focus of this chapter is on North American bison, but it should also be applicable to European bison.

Bison can be extremely difficult to anesthetize. Major complications of anesthesia can include: hypoxemia, bloat, regurgitation, and hypoxemia. Bison are also predisposed to the development of capture myopathy, which can occur during or after anesthesia.

PRE-ANESTHETIC CONCERNS

Bison are similar to domestic cattle in many respects anesthesia of an animal with a full rumen pack can result in bloat or regurgitation. Xylazine or general anesthesia with volatile agents will lead to decreased rumen motility, bloat, and regurgitation. These can be fatal complications and tend to be more severe in large, mature animals (Caulkett et al., 2000).

Ruminants are prone to hypoxemia during general anesthesia. Positioning in dorsal or lateral recumbency will exacerbate hypoxemia (Caulkett et al., 2000). α_2 -Agonist drugs such as xylazine or medetomidine also exacerbate hypoxemia (Caulkett et al., 2000).

Bison stress very quickly. Stressed animals tend to over-ride the sedative effects of α_2 -agonist drugs necessitating the use of relatively high dosages of these agents to produce recumbency. Stressed animals are prone to capture myopathy, the acute form of which is a shocklike syndrome that can result in death within hours.

The sub-acute form often results in muscle damage, myoglobinuria, and potentially kidney failure. The chronic form is characterized by severe muscle fibrosis, chronic progressive renal failure, and the possibility of muscle rupture in already weakened tissues (Spraker, 1993). Rupture of the gastrocnemius muscles is a common manifestation of exertional myopathy in bison. It can occur acutely or may manifest in the chronic form. It is extremely important to keep chase times to a minimum, and try to avoid excitement prior to induction (Figure 58.1).

Hyperthermia increases metabolic oxygen demand and increases the risk of capture myopathy. If immobilization is anticipated, it should be planned for the cool hours of the day. Field immobilizations should probably not be conducted when ambient temperatures exceed 23°C.

Trauma during induction of anesthesia is not uncommon. It is particularly important to control the rest of the herd during induction as other members of the herd may traumatize the drugged animal. In particular attendant bulls may mis-read gait and behavior patterns during the induction phase and attempt to mount ataxic females.

There is no information concerning the abortogenic effects of xylazine in bison cows. The risk of abortion in the last third of pregnancy may be increased with this drug.

MONITORING AND SUPPORTIVE CARE

Pulmonary Function

Hypoxemia can be severe during anesthesia. Hypoxemia, in the face of hyperthermia, is a particularly serious situation, as hyperthermia increases tissue oxygen demand. This can increase the risk of capture myopathy or result in acute mortality. Hypoxemia can be prevented or treated in the field. Animals should be positioned in sternal recumbency. The head and neck should be



Figure 58.1. Aerial darting of a plains bison, pursuit times should be limited to less than 2 minutes whenever possible.

extended to maintain a patent airway. The animal should be monitored for hypoxemia, ideally with a pulse oximeter. A multi-site sensor applied to the tongue generally provides a good signal. Normal hemoglobin saturation should be 95% to 98%, and saturation below 85% is considered hypoxemic. If a pulse oximeter is not available, the mucous membranes should be monitored for cyanosis. Severely hypoxemic animals are often tachycardic. Heart rates above 150 in bison may result from a stress response owing to hypoxemia, hypercarbia, pain, or hypotension. Tachycardia, followed by severe bradycardia (heart rate less than 30) is often a warning sign that the degree of hypoxemia is critical and the heart may fail. Supplemental inspired oxygen should be considered in hypoxemic animals (Caulkett et al., 2000). Portable equipment is available to facilitate oxygen delivery. An ambulance-type regulator and aluminum D-cylinder is lightweight, portable, and sturdy. It can provide a 10 l/minute flow for up to 30 minutes. An E-cylinder provides this flow for an hour or more. A nasal catheter is a simple method to provide supplemental inspired oxygen. The catheter should be threaded as far as the medial canthus of the eye. A flow rate of 10 to 15 l/minute is required in bison (Figure 58.2).

Arterial blood gas analysis provides the most accurate means of assessing oxygenation. The femoral artery may be used in laterally recumbent animals. It is prudent to exercise caution when working near the legs of anesthetized bison as they may spontaneously kick. The coccygeal artery can be used to facilitate arterial blood sampling in sternally recumbent bison (Figure 58.3).

Cardiovascular System

Heart rate and pulse quality should be monitored every 5 minutes. The auricular pulse is difficult to palpate in bison. The facial artery or the femoral artery may be used. Bison anesthetized with xylazine-telazol or



Figure 58.2. Plains bison positioned in sternal recumbency.



Figure 58.3. Collection of an arterial blood sample from the coccygeal artery of a sternally recumbent bison.

medetomidine-telazol have an average heart rate of approximately 60 bpm (Caulkett et al., 2000). Bison anesthetized with carfentanil-xylazine have a slightly higher heart rate. An average heart rate of 75 beats per minute (bpm) has been reported with carfentanil-xylazine (Kock and Berger, 1987; Haigh and Gates, 1995).

Body Temperature

Rectal temperature should be monitored every 5 to 10 minutes. Bison are prone to hyperthermia, particularly following a long pursuit. Rectal temperatures greater than 40°C are cause for concern, and attempts should be made to cool the animal; cold water sprayed on the animal or snow packed into the inguinal and axillary regions may help. Rectal temperature in excess of 41°C is an emergency and should be treated aggressively. It is difficult to actively cool large animals and often the best

option with severe hyperthermia is to antagonize the immobilizing agents and allow the animal to recover. Hyperthermia greatly increases metabolic oxygen demand. Hyperthermia, in the face of hypoxemia, is a particularly serious complication. Hyperthermic animals should receive supplemental inspired oxygen to offset hypoxemia.

Supportive Care

Maintenance in sternal recumbency helps to prevent the development of ruminal tympany. If ruminal tympany is a problem, the animal may be rocked gently to stimulate eructation. A rumen tube can be used, but may predispose to regurgitation and aspiration. Generally, if ruminal tympany is severe, it is advisable to finish the procedure quickly and antagonize the anesthetic agents. If α_2 -agonists have been used, the administration of tolazoline or atipamezole will stimulate ruminal activity and relieve ruminal tympany.

Endotracheal Intubation

Intubation is not typically performed in field settings, but it is recommended if the bison is to be maintained on volatile anesthesia. The technique is the same as for cattle. The bison is maintained in sternal recumbency. A mouth gag is placed prior to intubation. The tongue is pulled forward and the distal end of the tube is held. The person performing the intubation advances his or her arm into the oral cavity and guides the tube to the epiglottis. The epiglottis is displaced ventrally with a finger, and the tube is advanced into the glottis. A mature bison requires a size 24 to 30 endotracheal tube. The head needs to be elevated to facilitate intubation. This can be difficult in large, mature animals, as the head can be heavy.

SEDATION AND ANESTHESIA OF CAPTIVE BISON

Bison restrained in a head gate and squeeze can be sedated with IV xylazine. The tail vein is useful for the injection of small volumes. Xylazine can be used as the sole agent at a dose of 0.1 to 0.2 mg/kg IV for standing sedation. Sedation may be enhanced by the addition of 0.05 mg/kg of acepromazine or 0.05 mg/kg of butorphanol administered IV. All three drugs may also be combined to produce deep sedation, and possibly recumbency. If short-term general anesthesia is desired, 0.2 to 0.5 mg/kg of xylazine can be administered IV via the tail vein to produce recumbency. This is followed by 2 mg/kg of ketamine via the jugular vein. If the jugular vein is used the head must be adequately restrained to avoid injury to handlers.

Anesthesia may be prolonged with 5% guaifenesin and additional 1 mg/kg boluses of ketamine administered to effect. Use guaifenesin cautiously as we have observed guaifenesin toxicity in two bison, at what appeared to be

a relatively low dose. It is premature to say these animals are overly sensitive to the drug, but it should be used cautiously until more information is available.

Xylazine should be antagonized at the end of the procedure. If IV ketamine has been used, the antagonist should not be administered for 10 to 15 minutes to avoid undesirable effects of the ketamine.

Bison calves can be induced to anesthesia with IV ketamine 2 to 4 mg/kg plus diazepam 0.2 mg/kg. This combination gives 5 to 10 minutes of light anesthesia. In depressed calves diazepam 0.2 mg/kg + 0.1 mg/kg of butorphanol can be used IV for sedation. If the calf is difficult to work with 0.1 to 0.2 mg/kg of xylazine + 0.1 mg/kg of butorphanol can be administered IM prior to induction with ketamine-valium.

IMMOBILIZATION OF FREE-RANGING BISON

Bison may require immobilization for a variety of reasons. Remote delivery of immobilizing agents necessitates the use of potent agents that can be delivered in relatively small volumes.

Xylazine-Ketamine

This combination can be a viable option for immobilization of bison: 0.5 to 1 mg/kg of xylazine may be combined with up to 4 mg/kg of ketamine. The major disadvantage of this combination is that it must be delivered in a large volume if commercial preparations are used. A large bull may require 5 to 10 ml of xylazine + 40 ml of ketamine. A further drawback of this combination is that premature antagonism of the xylazine can result in rigidity and convulsions from the ketamine.

Carfentanil-Xylazine

This combination has been used for capture of freeranging wood and plains bison (Kock and Berger, 1987; Haigh and Gates, 1995). Carfentanil is administered at a dose of 4 to 8 µg/kg, this is combined with xylazine, at a dose of 0.05 to 0.1 mg/kg. Bison, like other ungulates, demonstrate increased activity and excitement during induction. If the animal demonstrates head and/or limb movement when approached after becoming recumbent an additional 0.05 to 0.1 mg/kg of xylazine may be administered IV to improve muscle relaxation. Following the procedure carfentanil should be antagonized with naltrexone at a ratio of at least 100 mg naltrexone per 1 mg of carfentanil. Naltrexone has been shown to be the drug of choice for antagonism of carfentanil in bison. Antagonism of carfentanil with naloxone has resulted in a high incidence of mortality from re-narcotization. Naltrexone has a long half-life and the incidence of re-narcotization is very low.

Complications of immobilization can include: hypoxemia, hypoventilation, regurgitation, and hyperthermia. Renarcotization is not usually a problem if naltrexone is used to antagonize carfentanil.

The major advantage of this combination is that it can be administered in very small volumes and produces reliable immobilization. It is a particularly attractive combination for wild animals, as decreased volume requirements improve the accuracy of dart placement and decrease tissue trauma.

Xylazine-Telazol

We have been using a dose range of 0.75 to 1.5 mg/kg of xylazine, combined with 1.5 to 3 mg/kg of telazol to induce immobilization of bison (Caulkett et al., 2000). The low end of the dose is often effective in calm animals. The high end of the dose range may be required in fractious or wild animals. A 400-kg cow could require a dose volume of up to 7 ml, which can decrease dart accuracy and increase tissue trauma. Large volume requirements decrease the utility of this mixture for wild animals, but it is still very useful in captive or game farmed animals.

The mixture produces approximately 1 hour of anesthesia, and provides adequate analgesia for minor procedures. The major complications that can be encountered with this combination are hypoxemia, bloat and/or regurgitation, and hyperthermia.

Xylazine should be antagonized following the procedure. Since the telazol dose is relatively low recoveries are generally smooth. Rougher recoveries may be noted if a high dose of telazol was used for induction. Tolazoline or atipamezole should be used to antagonize xylazine in bovids. Tolazoline can be administered at a dose of 2 to 3 mg/kg. This dose may be split between IV and IM administration. Yohimbine does not effectively antagonize xylazine-induced sedation in bovids and should not be used as the reversal agent (Klein and Klide, 1989).

Medetomidine-Telazol

The immobilization characteristics of this combination are similar to those of xylazine-telazol (Caulkett et al., 2000). The major advantage of medetomidine-telazol is that it can be administered at approximately half the volume of xylazine-telazol. This quality greatly increases its utility in free-ranging animals. Another major advantage is that a lower dose of telazol is required and arousal from sedation is significantly faster than recovery following antagonism of the xylazine in the xylazine-telazol mixture.

We have used this combination at a dosage of 60 μ g/kg of medetomidine + 1.2 mg/kg of telazol to induce immobilization in captive and free-ranging bison. Medetomidine can be antagonized with 180 mg/kg of atipamezole. Caution should be observed following antagonism of the medetomidine as arousal from anesthesia can be very rapid, and IV administration of atipamezole should be avoided unless the condition of the animal is seriously compromised.

Complications are similar to those of xylazinetelazol and include hypoxemia, hypercarbia, and ruminal tympany. Steps should be taken to prevent or treat these complications.

Medetomidine-Ketamine

This combination has been used for immobilization of captive European bison. The effective dose is 2.5 mg/kg of ketamine plus 0.08 mg/kg of medetomidine (Jalanka and Roeken, 1990).

Xylazine-Hydromorphone-Telazol

This combination has been developed to address some of the adverse effects of xylazine-telazol alone. The addition of hydromorphone to this combination decreases the telazol and xylazine requirements. The mean dosage administered to plains bison was 1.98 mg/kg of telazol, 0.26 mg/kg of hydromorphone, and 1.32 mg/kg of xylazine. Reversal of sedation was achieved with 4 mg/kg of tolazoline and 0.09 mg/kg of naltrexone (Shury and Caulkett, 2006). Preliminary results indicate that this mixture induces less hypoxemia than xylazine-telazol alone and reversal of sedation is more rapid following the administration of antagonists. This combination is promising in bison and other ungulates.

Volatile Anesthesia

Volatile anesthesia may be used for prolonged procedures. Isoflurane is preferable to halothane as it is less arrhythmogenic. Induction can be achieved with IV xylazine-ketamine or xylazine-guaifenesin-ketamine in restrained animals, or IM xylazine-telazol in unrestrained animals. It is very important to fast animals for 24 to 48 hours prior to general anesthesia as bovids are particularly prone to bloat and regurgitation during volatile anesthesia.

Animals under 150 kg can be anesthetized with a small animal machine. Animals over 150 kg require a large animal circuit.

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59

Lagomorphs (Rabbits, Hares, and Pikas)

Darryl J. Heard

INTRODUCTION

The order Lagomorpha includes 91 living species distributed among two families: Leporidae (rabbits and hares) and Ochotonidae (pikas) (Wilson and Reeder, 2005). Lagomorphs are herbivores, closely related to rodents (Nowak, 1999). Adults have two pairs of upper incisors; the smaller second is located directly behind the first. Pikas are small (125–400 g) with short ears and legs, and no visible tail (Nowak, 1999). Rabbits and hares have elongated ears and legs, and rely on speed to escape predators. Pikas are found in northern Eurasia and western North America. The sexes are equal in size, and their fur is long and dense (Nowak, 1999). Despite enduring severe winters they do not appear to hibernate.

The term hare is restricted to animals of the genus *Lepus* (Nowak, 1999); all other leporids are rabbits. Hares are usually larger and have black ear tips. Young rabbits are born blind, naked, and helpless in a fur-lined nest. In contrast, hares are born fully furred in the open with eyes open and capable of running in a few minutes (Nowak, 1999). Leporids weigh 400 to 7,000 g; females are usually larger than males (Nowak, 1999). Frightened or captured rabbits may emit loud, shrill screams.

The literature is dominated by parenteral anesthetic regimens for research rabbits (and rodents). Great care must be taken in selecting regimens for clinical cases or free-living animals based on this information. This is because the goals of research anesthesia are often not the same (i.e., prolonged immobility and not necessarily recovery). Similarly, anesthetic regimens have improved in safety, analgesia, and efficacy as new drugs have become available; older anesthetic references must be critically interpreted.

The European rabbit (*Oryctolagus cuniculus*) is a popular pet, as well as food and fur animal, and one of the most common research mammals. Consequently, the following discussion emphasizes this species. Pikas are similar to rodents in form and size, and anesthesia is the same.

PHYSICAL RESTRAINT

Domestic rabbits are not aggressive. However, some animals bite and scratch, particularly those used in research. Rabbits and hares have long legs for leaping and running, and explosively kick when restrained. The kick force is sufficient to fracture the lower thoracolumbar vertebrae. Distal tibial fractures are common if a rabbit falls. Leg fractures also occur in wire-bottom cages when a toe or leg is caught. Leporids must not be held by the ears. They can be grasped by the nape for short periods, but it is important to support the rump. When carrying for a distance they are either placed in a transport cage or cradled in one arm with their head tucked into the body of the handler.

Physical restraint devices (e.g., rabbit squeeze boxes, cat bags, etc.) are a useful adjunct to anesthesia, particularly in the induction period. However, restrained rabbits quickly develop hyperthermia. Physical restraint of free-living rabbits and hares is minimized; chemical immobilization or inhalation anesthesia is recommended for examination and sample collection.

PREANESTHETIC PREPARATION

Assessment of patency of the nares and nasopharynx is essential, especially when an inhalant anesthetic mask is used. Lagomorphs are primary or obligate nasal breathers, and upper respiratory disease is common (e.g., snuffles).

This author does not recommend fasting since leporids do not regurgitate or vomit. Fasting has also been recommended to reduce gastrointestinal volume and, thereby, diaphragmatic and lung compression. However, it is unlikely to significantly reduce volume in an herbivore and may cause ileus.

Premedication always includes an analgesic plan; recommended premedication dosages are given in Table 59.1. Routine use of parasympatholytics is

Table 59.1. Drug dosages (mg/kg, IM, SC or IV) for premedication and sedation of rabbits.

Drug	Dosage	Comments
Acepromazine Diazepam	0.1-1.0 1.0-5.0	Healthy, hemodynamically stable animals, will produce hypotension. Peak effect may take \geq 45 mins.
Midazolam Xylazine	1.0-2.0 1.0-5.0	Higher dosages associated with marked cardiopulmonary depression and bradyarrhythmias.
Atropine Glycopyrrolate	0.8-1.0 0.1	Use in emergencies, not recommended for routine premedication.

Adapted, in part, from Mason DE. Anesthesia, analgesia and sedation for small mammals. In: Hillyer EV, Quesenberry KE, eds. *Ferrets, Rabbits and Rodents. Clinical Medicine and Surgery.* Philadelphia: W.B. Saunders, 1997:378–391.

unnecessary and will alter gastrointestinal motility. Many, but not all rabbits have circulating levels of atropine esterases. Higher atropine dosages in these animals increase the likelihood of a therapeutic effect, but also toxicosis. In rabbits, atropine sulfate (0.2–2.0 mg/kg) only briefly induced a moderate tachycardia, but glycopyrrolate (0.1 mg/kg) elevated heart rate for greater than or equal to 50 minutes (Olson et al., 1994).

Acepromazine has similar effects as in other domestic mammals. It is used only in healthy hemodynamically stable animals. Peak effect is not attained for 30 to 45 minutes, even when administered IV. Tranquilization is inversely related to the amount of environmental stimulation. Benzodiazepines provide good sedation and relaxation. They are a useful adjunct to induction of debilitated patients because of their minimal cardiopulmonary effects and they can be reversed with flumazenil. Xylazine, detomidine, or medetomidine are usually not used alone for sedation.

ANALGESIA

The principles and techniques for small mammal analgesia are well reviewed by Robertson (2001), Flecknell (2001), and Machin (see Chapter 3). Recommended rabbit dosages are given in Table 59.2.

LOCAL AND REGIONAL ANESTHESIA

Rabbits are models for epidural and intrathecal administration of local anesthetics and analgesics (Kero et al., 1981; Hughes et al., 1993; Taguchi et al., 1996; Pang et al., 1999). Local and epidural anesthesia are used for minor and occasionally major (e.g., Caesarian section) procedures, respectively. Recommended epidural volume administered by the lumbosacral space is 0.2 ml/kg. Using this dosage the rank order for onset of action and duration of effect was 2% lignocaine, 2% lignocaine with adrenaline (1:200,000), and 0.5% bupivacaine (Hughes et al., 1993).

Local anesthetics have a low therapeutic index (e.g., bupivacaine) and commercial preparations contain concentrations appropriate to humans. Consequently, care must be taken to calculate and prepare appropriate volumes for infiltration. For example, if the toxic dose of

Table 59.2. Analgesic drugs dosages (mg/kg) used in rabbits and hares.

0.01-0.05 IM, SC, IV q6-12h
0.1-0.5 IM, SC q4h
10 IM, SC q2-3h
2–5 IM, SC q4h
0.05-0.2 IM, SC q8-12h
4 IM, SC q24h, 1.5 PO q12h
1–2 IM, SC q12h
3 IM, SC q24h
0.2 IM, SC, 0.3 PO q24h

Adapted from Flecknell PA. Analgesia of small mammals. North Am Vet Clin Exotic Anim Pract 2001:4:47–56; Mason DE. Anesthesia, analgesia and sedation for small mammals. In: Hillyer EV, Quesenberry KE, eds. Ferrets, Rabbits and Rodents. Clinical Medicine and Surgery. Philadelphia: W.B. Saunders, 1997:378–391.

lidocaine is 10 to 20 mg/kg, the equivalent volume of a 2% lidocaine solution would be less than 0.5 to 1.0 ml/kg.

PARENTERAL ANESTHESIA

Rabbits and other lagomorphs have evolved the ability to detoxify many ingested plant chemicals. For example, circulating atropine esterases in many breeds are capable of inactivating belladonna alkaloids. A high metabolic rate also implies rapid metabolism and excretion of parenteral drugs. Consequently, they generally have a shorter duration of effect than comparable doses in larger mammals.

Drug Administration

Injection routes include subcutaneous, intramuscular, intraperitoneal, intravenous, and intraosseous. This author prefers intramuscular (IM) injections in the quadriceps muscle. The rabbit is held on a table with its head tucked into the arm of the holder. The muscle is held with one hand and the other hand makes the injection from the front.

Potentially irritant solutions (e.g., high or low pH solutions) are not administered subcutaneous (SC) or IM because of the risk of self-mutilation (Beyers et al., 1991). This can be reduced by diluting the solution, avoiding large volume injections, and injecting in the large

proximal leg muscles. The author recommends intraperitoneal (IP), rather than IM or subcutaneous (SC), injections in pikas because of their small size.

Intranasal administration of some analgesics, sedatives, and anesthetics is an effective and rapid route in rabbits (Robertson and Eberhart, 1994; Lindhardt et al., 2001).

Drugs

Ketamine has a very short duration of clinical effect owing, in part, to redistribution and renal elimination (Bjorkman and Redke, 2000). Consequently, renal impairment markedly prolongs recovery. Xylazine and other α_2 -adrenergic agonists are frequently combined with ketamine for short-term immobilization and surgical anesthesia. These combinations, particularly at the higher dosage levels, produce mild to severe dosedependent hypotension, bradyarrhythmias, and respiratory depression, with associated hypercapnia, acidemia, and hypoxemia. As with all parenteral anesthetic regimens, some form of oxygen supplementation and assisted ventilation is recommended. Ketamine/benzodiazepine combinations produce less cardiopulmonary depression and analgesia, but good muscle relaxation.

In Dutch belted rabbits multiple anesthetic episodes with ketamine/xylazine (50/10 mg/kg IM) were associated with myocardial necrosis and fibrosis (Marini et al., 1999). Similarly, in New Zealand white rabbits, detomidine, alone and in combination with ketamine or diazepam, produced the same injury (Hurley et al., 1994). The postulated mechanism was decreased coronary blood flow. However, other causes (e.g., hypovitaminosis E, excessive anesthetic dosage, and hypoxemia) were not ruled out.

Tiletamine/zolazepam is not recommended for use. This combination requires very high dosages (32–64 mg/kg) to produce immobility to noxious stimuli (Brammer et al., 1991). These dosages also produce dose-dependent renal tubular necrosis within 7 days of injection (Brammer et al., 1991).

Propofol is used for induction and maintenance. Its effects are similar to those described in domestic animals (Aeschbacher and Webb, 1993). The total induction dose is dependent on administration rate. Propofol alone produces inadequate analgesia for painful procedures, and anesthetic maintenance with infusions is not recommended unless cardiopulmonary support is provided. It is indicated for induction of healthy animals in which vascular access can be attained prior to anesthesia. A slow infusion can also be used for sedation to facilitate mask induction. Animals should be intubated and ventilated as soon as possible after induction.

INHALATION ANESTHESIA

Inhalation anesthesia with either isoflurane or sevoflurane is the primary component of most anesthetic regimens. It allows rapid induction, recovery, and control of anesthetic depth, whereas adverse effects are dose dependent and reversible.

Immediately after induction rabbits often have shallow rapid respirations and decreased alveolar ventilation. This delays attainment of maintenance alveolar anesthetic levels, and may explain the need for high isoflurane vaporizer settings (4%–5%) in spontaneously breathing rabbits. Premedication and assisted endotracheal intubation ameliorate this. Intubation allows assisted ventilation, improved alveolar ventilation, and thus better control of anesthesia.

Induction

Inhalant anesthesia is used either alone or as an adjunct to induction. The anesthetic is administered into an induction chamber or through a mask. The advantage of a chamber is the animal is not physically restrained during the involuntary excitement phase of induction. This reduces the risk of injury to both handler and patient. Disadvantages include environmental contamination and difficult monitoring.

Mask induction of restrained animals is not recommended. Anesthetic chambers and masks are clear to see the patient. The chamber top is secured to prevent the animal escaping. Inhalant anesthetic is introduced through one opening and waste gas removed from another. The vaporizer is set at maximum concentration and oxygen flow rate at 2 to 4 L/minute. Once the animal loses its righting response (usually 5–10 minutes) it is removed from the chamber and a mask placed over its nose and mouth. The chamber is placed outside or closed to allow waste gases to be safely voided. The animal is either maintained with a mask or intubated.

When using a mask the animal's head and neck is kept in extension to prevent obstruction to breathing. Respiratory pattern, rate, and noise are assessed. If there appears to be difficulty in breathing the head and neck are moved to correct the obstruction. If not, cotton-tipped applicators are used to clear the oropharynx and nares. If this fails to relieve the problem, the animal is intubated or awakened.

Endotracheal Intubation

In clinical practice intubation of rabbits should be a routine standard of care, especially for complex and prolonged procedures. Maintenance with a mask allows more inhalant anesthetic gas contamination of the environment, and does not allow assisted ventilation. Pediatric laryngeal mask airways are easier to position, but are associated with increased waste gas exposure and stomach inflation during ventilation (Smith et al., 2004).

Endotracheal tube size ranges from 2 to 4 mm ID. They are preferably clear to see condensation or occlusion with mucous and blood. In rabbits it is essential that the animal's head and neck are moderately

hyperextended to align the larynx and trachea with the oropharynx. The epiglottis must be displaced ventral to the soft palate for visualization of the glottis through the oropharynx. Regardless of technique, the rabbit is relaxed before intubation. This is indicated by absence of a response to either an ear or toe pinch.

There are two techniques: blind and direct visualization. An additional technique, not recommended because of laryngeal and tracheal trauma, uses retrograde placement of a guide wire or catheter through the larynx and out through the mouth. The endotracheal tube is then passed over the wire into the larynx. This technique is indicated for respiratory arrest when direct visualization fails.

This author prefers the blind technique for routine intubation. However, it requires breathing to guide endotracheal tube placement. The rabbit is placed in sternal recumbency on a table at a height comfortable for the anesthetist. If you are right handed, stand on the right side of the animal and grasp the head with the left hand. The head is grasped from above and behind with the thumb and little finger under the mandibular ramus. Alternatively, some find aligning the head and neck horizontal and parallel to the table also allows intubation. Although this author has used this position, it makes it awkward to listen and manipulate the tube.

The endotracheal tube is inserted between the incisors and first premolar, and passed over the tongue base. The head and neck are lifted into hyperextension, and the anesthetist places her or his ear to the tube. The tube is advanced toward the glottis until respiratory noise is loudest. No or gurgling sound indicate the tube is in the esophagus. The tube is repetitively and gently advanced to the glottis until it enters the trachea. At the point of peak noise it helps to rotate the endotracheal tube 180 degrees to displace the epiglottis. Local anesthetic, both as a gel applied to the end of the tube or a liquid poured down the tube, desensitizes the glottis and facilitates intubation. The rabbit may forcefully cough the tube out. Do not persist in intubation attempts for more than a few minutes, or when there is evidence of either laryngeal edema or hemorrhage.

The direct visualization technique is similar. An assistant opens the animal's jaws using gauze tape placed around the upper and lower incisors. The tongue is grasped by gauze square and pulled up and to the side. A cotton-tipped applicator may assist grabbing the tongue. A laryngoscope with a pediatric straight blade (Miller #0 or #1) is inserted into the oropharynx, the head and neck are hyperextended, and the epiglottis is displaced. The endotracheal tube is passed down the laryngoscope blade and through the glottis; sight of the glottis is usually lost as the endotracheal tube occludes the oropharynx. Alternatively, a small-diameter catheter is placed as a guide for the tube. In large rabbits the tube can also be placed over a rigid endoscope used to visualize the glottis (Tran et al., 2001). Once in place the tube

is advanced into the glottis. Placing the rabbit in dorsal recumbency may facilitate glottal visualization.

If unsure that the tube is in the correct place, remove it and reassess placement. A pulse oximeter is invaluable for monitoring potential oxygenation problems caused by airway obstruction. Correct tube placement is determined by: (1) seeing condensation on a metal surface placed at the end of the tube or on the inside of the tube; (2) detecting air movement with hair placed in front of the tube; (3) watching the non-rebreathing bag; (4) the response to intubation (coughing etc.); or (5) detection of exhaled carbon dioxide on a capnograph. To insure the tube has not been placed into a single bronchus, premeasure the tube before use, and auscultate both lung fields for respiratory sounds after intubation.

PERIOPERATIVE MONITORING

Anesthetic Depth

In rabbits anesthetized with isoflurane, the eyelid aperture increased in a predictable dose-dependent manner (Imai et al., 1999). This response cannot be evaluated in the clinical patient because the cornea is protected with either a lubricant or the eyelids are taped closed. The eyeball rotates medially, then either dorsally or ventrally at 0.8 isoflurane MAC before becoming centrally fixed at greater than 1.5 MAC (Imai et al., 1999). Palpebral and corneal reflexes are observed at 0.8 MAC, but are abolished at greater than 2.0 MAC. A fixed dilated pupil, unresponsive to light and with no corneal reflex is a cross-species indicator of either excessive anesthetic depth or brainstem hypoperfusion and ischemia. Anal tone is usually retained until deep anesthesia.

Evaluating physiological and muscular response to a painful stimulus assesses pain and nociceptor response. This can be a toe, ear, and/or tail pinch, or skin incision. Increasing depth toward a surgical plane of anesthesia is assumed when muscle tone (e.g., jaw muscle, anal sphincter) decreases, palpebral and corneal reflexes are obtunded, and respiration pattern becomes regular and even. Sudden tachycardia, hypertension, and tachypnea in response to stimuli are indicative of inadequate anesthetic depth or analgesia.

Cardiovascular

An esophageal stethoscope can be used to monitor heart rate in the intubated anesthetized patient. Alternatively, a quality pediatric stethoscope is used. The electrocardiograph should have a multichannel oscilloscope with non-fade tracing and freeze capabilities. Additionally, it must be able to record at speeds of 100 mm/second and amplify the signal to at least 1 mV equal to 1 cm. Standard lead positions are used.

Placement sites for the Doppler flow probe include the ventral aspect of the tail base, the carotid, femoral, and auricular arteries, and directly over the heart. Sites for indirect blood pressure measurement include the legs, forearms, tail, and ears. The forelimb cuff oscillometric method is accurate for evaluation of arterial blood pressure at low and normal pressure ranges (Ypsilantis et al., 2005). Direct arterial blood pressure can be measured using a 22 to 24 over-the-needle catheter placed in the auricular artery in the center of the pinna (Ypsilantis et al., 2005).

Respiratory

Respiration rate (RR) is inversely related to bodyweight and is determined by evaluating either thoracic wall or reservoir bag movement. As with cardiac auscultation, evaluation requires a good-quality stethoscope with appropriate head and length of tubing, and an experienced ear. The esophageal stethoscope can be used to evaluate respiratory noise. However, there is more likely to be artifactual noise that must be distinguished from true respiratory noise. Arterial blood gas samples are obtained from any palpable artery; the femoral, metatarsal, and auricular arteries. Infiltration of the periarterial area with 1% lidocaine without epinephrine may prevent reflex vasoconstriction.

Pulse oximetry has been evaluated in rabbits and appears accurate at hemoglobin saturation levels greater than 85% (Vegfors, 1991). Potential sites for placement of transmission pulse oximeter sensors include the ear, tongue, buccal mucosa, paw, vulva, prepuce, and proximal tail. Surprisingly, in rabbits the tail base and paws appear more effective than the ears. This may be caused by excessive compression of the aural vasculature by the clamp holding the probe. A reflectance pulse oximeter sensor is used in the esophagus or rectum, or applied to the skin surface on the ventral neck overlying the carotid artery.

Thermoregulatory

Hypothermia is common; body temperature measurement is a standard of care during all procedures. It is preferably measured continuously. For measurement of core body temperature, it is necessary to use a temperature probe attached to an esophageal stethoscope.

PERIOPERATIVE SUPPORTIVE CARE

The eyes of rabbits and hares are prominent and care must be taken to prevent corneal injury during positioning. It is important to place ophthalmic ointment at the beginning of and during a procedure, and make sure the eyelids are closed.

Cardiovascular

Vascular access is established in physiologically unstable patients and those likely to decompensate from hemorrhage, endotoxemia, etc. during the perianesthetic period. Potential catheterization sites include the cephalic, saphenous, and auricular veins. Catheters should not be placed in the central auricular artery

(except for blood pressure monitoring) because of the risk of thrombosis and ischemic necrosis of the ear. Penetration of the skin before placement, with either a hypodermic needle or scalpel blade, is done to prevent catheter buckling. Intraosseous catheter sites include the proximal femur, tibia, and humerus. Subcutaneous fluid administration is the least appropriate route for correction of deficits or replacement from hemorrhage.

Respiratory

General anesthetics produce ventilatory depression. This effect may be either additive or synergistic with underlying disease resulting in marked hypercapnia and/or ventilatory arrest. High-inspired oxygen concentrations also decrease ventilatory drive. Ventilation is also affected by body position and compression of the respiratory exchange tissues by distended viscera and/or obesity. Inadvertent compression of the chest by surgeons is common in small patients. Developing good hand position techniques, an attentive anesthetist, and the use of clear plastic drapes helps prevent this. Rabbits have very small chest cavities relative to body size and have a high prevalence of respiratory disease. Additionally, they often develop tachypnea under anesthesia with a normal to decreased alveolar ventilation.

Adequacy of ventilation is most accurately assessed using PaCO₂. Visualization of chest wall movement is a deceptive guide to adequacy of ventilation. Consequently, the author recommends either assisted or controlled ventilation of intubated patients under general anesthesia. Doxapram is not recommended for use in hypoventilating patients unless anesthetic reversal, or intubation and mechanical ventilation are impossible or contraindicated.

Thermoregulatory

Minimizing anesthesia time and using warm surgical preparation solutions, wrapping the body, increasing the room temperature, and using external heat sources (i.e., circulating warm water blankets and forced air warmers) reduces hypothermia. Electric heat blankets are not used because they have the potential to cause severe burns. Similarly, heated fluid bags placed in contact with the skin may cause burns.

RECOVERY

Recovery is a critical period during which the patient is placed in a warm, quiet environment and monitored. Supportive care established during anesthesia is continued until the patient is fully alert and stable. In particular, vascular access is maintained to allow emergency administration of drugs and fluids.

The anesthetic drugs used, duration of procedure, and the magnitude of physiological dysfunction incurred determine duration and quality of recovery. Prolonged recovery is usually owing to hypothermia,

Table 59.3. Drugs used for induction and maintenance of anesthesia in rabbits (and hares).

Drug or Drug Combination Parenteral	Dosage	Route	Comments	References
Acepromazine/ketamine Xylazine/ketamine	0.1/25-40 mg/kg 3-5/20-40 mg/kg	IM, IV IM, IV	Hypotension Sometimes marked cardiopulmonary depression. Duration of effect decreased with yohimbine (0.2 mg/kg IV).	Borkowski et al., 1990; Henke et al., 2005; Hobbs et al., 1991; Lipman et al., 1987, 1990; Sanford and Colby, 1980
Diazepam/ketamine	1-5/20-40 mg/kg	IM, IV		,,
Midazolam/ketamine	1/20-40 mg/kg	IM, IV		
Zolazepam/tiletamine	5–25 mg/kg	IM, IV	This dosage does not provide complete immobility or surgical anesthesia. Very high dosages associated with nephrotoxicity.	Brammer et al., 1991
Xylazine/zolazepam/ tiletamine	5/15 mg/kg	IM	Cardiopulmonary depression, surgical anesthesia, prolonged duration of effect.	Polpilskis et al., 1991
Medetomidine/ketamine	0.5/35 mg/kg	IM, IV	Combined with buprenorphine 0.03 mg/kg, animals intubated, ventilated and maintained with isoflurane.	Difillipo et al., 2004; Orr et al., 2005
Propofol	3–6	IV		
Inhalant				
Halothane	Induction 5%, Maintenance 1%–2%			
Isoflurane	Induction 5%, Maintenance 2%–3%			
Sevoflurane	Induction 7%–8%, Maintenance 3%–4%			

hypoglycemia, and anesthetic overdose or impaired drug elimination. Care is taken when rewarming an animal that is possibly hypovolemic and/or hypoglycemic, because warming results in dilation of vasoconstricted peripheral vessels, as well as increase metabolic demand for glucose.

FREE-LIVING LAGOMORPHS

Inhalation anesthesia is recommended for all wild lagomorphs because of rapid induction and recovery. Capture and placement into an induction chamber are relatively easy. Alternatively, the trap can be placed in the chamber or a plastic bag for inhalant anesthetic administration. Where inhalant anesthesia is not feasible, parenteral drug combinations are administered IM or IP (Table 59.3). Drug combinations that include either α -adrenergic agonists or benzodiazepines are potentially reversible (Table 59.3).

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60 Rodents Darryl J. Heard

INTRODUCTION

Rodentia includes the most living mammalian species, 2,277 (Wilson and Reeder, 2005). Although usually small (less than or equal to 200 g), several are very large (e.g., marmots, *Marmota*; giant squirrels, *Ratufa*; pacas, *Agouti*; maras, *Dolichotis*; capybara, *Hydrochaeris hydrochaeris*; beaver, *Castor*; and porcupines, *Hystrix*). Rodents are common pets and research animals, including the house mouse (*Mus musculus*), rat (*Rattus norvegicus*), chinchilla (*Chinchilla laniger*), Syrian and Siberian hamsters, guinea pig (*Cavia porcellus*), and gerbil. Rodents have four incisors, no canines, and there is a gap between the incisors and the cheek teeth (Nowak, 1999). Some have cheek pouches, internal or external, that open near the angle of the mouth (Nowak, 1999). During anesthesia these pouches can be a source of aspirated food material.

CONSEQUENCES OF SMALL BODY SIZE

Schmidt-Nielsen (1984) well describes the relationship between body size and vertebrate physiology. As small animals rodents have high metabolic and oxygen consumption rates; therefore, low tolerance to even brief hypoxemia. Irreversible central nervous system injury occurs within less than or equal to 30 seconds of respiratory arrest. Increased oxygen uptake requires increased alveolar ventilation resulting in more rapid inhalant anesthetic uptake and excretion. High metabolic rates increase the speed of elimination of parenteral drugs. In herbivores this is enhanced by adaptations for detoxification of chemicals in their food. Consequently, drugs have shorter duration of effect than in larger mammals and require higher dosages.

High metabolic rates and small glycogen reserves predispose to hypoglycemia. A small body has a large surface area to volume ratio, and often higher temperature. Convective heat loss is rapid and hypothermia assured unless supplemental heat is provided. Loss of even small amounts of blood may lead to hemorrhagic

shock and death. Airway resistance is inversely related to radius; slight changes in diameter (e.g., from edema and mucous accumulation) have a dramatic effect on respiratory work.

ZOONOTIC DISEASES

Many species harbor pathogens that infect humans (Padovan, 2006). Handling rodents awake is minimized to prevent bites and scratches. The use of physical barriers (i.e., gloves, breathing masks, and biological hazard suits) is based upon the predetermined risk, species, and procedure.

PHYSICAL RESTRAINT

Capture techniques for free-living rodents are described by Barnett and Dutton (1995). All rodents bite, including many kept as pets. In an animal of unknown temperament, inhalant anesthesia is an acceptable alternative for physical examination. Care is taken with small rodents to avoid physical restraint in place of adequate analgesia and anesthesia. Large rodents are restrained in squeeze cages (see Chapter 12) or remotely injected for drug administration (see Chapter 4).

Pet rodents can often be gently picked up in the palm of the hand. Some rodents may be grasped at the tail base for transfer from cage to cage. This technique, however, is avoided in animals that shed their tails in response to a threat (e.g., spiny tailed mice) or are able to turn and bite (Nowak, 1999).

Grasping the nape is used to restrain some small rodents. Hamsters and others with loose skin require a very tight grasp to prevent them turning and biting (Figure 60.1). Small to medium-sized rodents are restrained with a hand around the neck and the thumb positioned under the jaw to prevent biting. In laboratory animal facilities mice and other small rodents can be transferred from cage to cage using soft forceps. This technique is also used for small free-living rodents



Figure 60.1. Some rodents (e.g., Siberian hamster) can be restrained by grasping the skin at the nape of the neck. However, sufficient skin must be grasped to prevent the animal from turning and biting the handler.

caught in traps. Leather or chain-mail gloves can be used to handle aggressive rodents, but they limit feel and the former do not protect against a direct bite.

Porcupines offer a unique challenge. Although they do not "shoot" their sharp quills, they back rapidly and with great force into a threat. The quills of New World porcupines have barbs that make their removal very difficult. The quills of all porcupines are covered in potentially pathogenic bacteria. They also make remote injection difficult. The author uses a purpose-built restraint box at the Central Florida Zoo to allow drug injection into the leg muscles of Southern African crested porcupines (*Hystrix africaeaustralis*) (Figure 60.2). The metal box has one side of wire with spaces sufficient to allow legs to drop through when the cage is turned. A leg is then grabbed and injected with a parenteral anesthetic. However, this porcupine has skin that tears very easily.

PREANESTHETIC PREPARATION

Rodents are primary or obligate nasal breathers and upper respiratory disease is common (e.g., pseudo-odontoma in prairie dogs, mycoplasmosis in rats). The nares are assessed for patency before induction with an inhalant anesthetic and mask. This author does not routinely remove food or water prior to anesthesia. Fasting exhausts glycogen stores. It may also contribute to ileus in guinea pigs and other herbivores.



Figure 60.2. A restraint cage for Southern African crested porcupines developed at the Central Florida Zoo. The cage is metal to prevent the animal from chewing. One side has large openings that cause the legs to fall through when the cage is turned. This allows an unprotected leg to be grasped and injected with immobilization drugs. Care must be taken in this species to prevent skin tearing.

PREMEDICATION

Recommended dosages are given in Table 60.1. In rats, atropine sulfate (0.05 mg/kg) and glycopyrrolate (0.5 mg/kg) increased heart rate for 30 and 240 minutes, respectively (Olsen, 1994). Although both reduce bradycardia in rodents anesthetized with ketamine/ α_2 -adrenergic agonist combinations, glycopyrrolate is more effective in maintaining heart rate within normal range (Olsen, 1994). Neither glycopyrrolate nor atropine influences respiration rate, core body temperature, or systolic blood pressure alone or combined with injectable anesthetics.

Benzodiazepines provide good sedation and relaxation and are a useful for induction of debilitated patients because of their minimal cardiopulmonary effects. Xylazine, and more recently medetomidine, is combined with ketamine to improve muscle relaxation, analgesia, and duration of effect. However, they produce respiratory depression and bradycardia. They are reversed with yohimbine, tolazoline, or atipamezole. Tolazoline (10–50 mg/kg), when compared with yohimbine (1 mg/kg), appeared most effective and safe for the reversal of xylazine/ketamine anesthesia in rats (Komulainen, 1991). In rats, yohimbine (20 mg/kg intraperitoneal [IP]) produced a high (22%) mortality.

ANALGESIA

The principles and techniques for rodent analgesia are reviewed by Machin (see Chapter 3), Robertson (2001), and Flecknell (2001). The two main groups of analgesic premedicants, opioids and non-steroidal anti-inflammatory drugs (NSAIDs), are combined or used alone. Even low-dosage ketamine provides analgesia and is worthwhile including, for this reason, in some

Table 60.1. Drugs and dosages (mg/kg) used for premedication in rodents.

Drug	Rat	Mouse	Gerbil	Hamster	Guinea Pig, Chinchilla, Prairie Dog	Beaver, Capybara, Porcupine
Acepromazine Diazepam Midazolam Xylazine Atropine	0.5-2.5 IM IP 3-5 IP PO 1-2 IP 10-15 IP 0.05 SC IM	0.5-2.5 IP 3-5 IM IP PO 1-2 IM IP 10-15 IP 0.05 SC IM	Not recommended 3–5 IP PO 1–2 IP 5–10 IP 0.05 SC IM	0.5-2.5 IM IP 3-5 IP PO 1-2 IP 5-10 IP 0.05 SC IM	0.5-2.5 IM 1-2.5 IM IP PO 1-2 IM IP 5-10 IP SC 0.05 SC IM	0.1 IM 0.1–1.0 IM PO 0.1–0.5 IM 1–5 IM SC 0.03 SC IM
Glycopyrrolate	0.01-0.02 SC IM	0.01-0.02 SC IM	0.01-0.02 SC IM	0.01-0.02 SC IM	0.01-0.02 SC IM	0.01 SC IM

From Flecknell PA. Anaesthesia and post-operative care of small mammals. *In Pract* 1991;13:180–189; Mason DE. Anesthesia, analgesia and sedation for small mammals. In: Hillyer EV, Quesenberry KE, eds. *Ferrets, Rabbits and Rodents. Clinical Medicine and Surgery*. Philadelphia: W.B. Saunders, 1997:378–391.

Use lower dosages for debilitated, geriatric, or obese animals and for those that are relatively large for the species. Acepromazine is not recommended for use in gerbils because it may lower the seizure threshold.

Table 60.2. Suggested analgesic dosages (mg/kg) for rodents.

Analgesic	Rat	Mouse, Gerbil, Hamster	Chinchilla, Guinea pig, Prairie dog	Beaver, Capybara, Porcupine
Buprenorphine	0.01–0.05 IM, SC q8–12h	0.05-0.1 SC q6-12h	0.05 IM, SC q6-12h	0.01–0.03 IM, SC q8–12h
Butorphanol	2 IM, SC q2-4h	1-5 SC q4h	2 IM, SC q4h	0.5 IM, SC q4h
Carprofen	5 IM, SC, PO q24h	5 SC q12h	4 IM, SC q24h	•
Flunixin	2.5 IM, SC q12h	2.5 SC q12h	2.5 IM, SC q12-24h	0.5 IM, SC q12-24h
Ketoprofen	5 IM, SC, PO q24h	?	?	1–3 IM, SC q 24h
Meloxicam	0.5–2 IM, SC, PO q24h	1-2 SC PO q12h	0.5 SC PO q12h	0.1-0.3 SC PO q12-24h
Meperidine	10-20 IM, SC q2-3h	10-20 SC q2-3h	10-20 IM, SC q2-4h	-
Morphine	2–5 IM, SC q4h	2–5 SC q4h	2–5 IM, SC q4h	1-3 IM, SC q4-6h
Oxymorphone	0.2-0.5 IM, SC q6-12h	0.2-0.5 SC q6-12h	0.2-0.5 IM, SC q6-12h	0.1 IM, SC q6–12h

From Flecknell PA. Anaesthesia and post–operative care of small mammals. *In Pract* 1991;13:180–189; Flecknell PA. Analgesia of small mammals. *North Am Vet Clin Exot Anim Pract* 2001;4:47–56; Mason DE. Anesthesia, analgesia and sedation for small mammals. In: Hillyer EV, Quesenberry KE, eds. *Ferrets, Rabbits and Rodents. Clinical Medicine and Surgery*. Philadelphia: W.B. Saunders, 1997:378–391.

anesthetic regimens (Robertson, 2001). Local and regional anesthesia (see the following) also has the potential to further enhance analgesia. Recommended dosages for analgesics are given in Table 60.2.

LOCAL AND REGIONAL ANESTHESIA

Many large captive species (e.g., guinea pig) are amenable to local and epidural anesthesia for minor and occasionally major (e.g., Caesarian section) procedures, respectively (Kero, 1981; Eisele, 1994). Most local anesthetics have a low therapeutic index (particularly the long-acting drugs such as bupivicaine) and commercial preparations usually contain drug concentrations suitable for humans. Consequently, great care must be taken to calculate and prepare appropriate volumes of local anesthetic for infiltration.

PARENTERAL ANESTHESIA

Small to medium-sized rodents are preferably induced and maintained with an inhalant anesthetic (see the following). Parenteral anesthetic regimens are used where inhalant anesthesia is not available (e.g., for field immobilizations), to reduce inhalant anesthetic pollution, to enhance analgesia, and for convenience in research facilities. Representative parenteral anesthetic regimens and dosages are described in Table 60.3.

Most published anesthetic regimens are designed for research animals. Unfortunately, the dosages and drugs are often not compatible with clinical practice or field work. They also assume animals are young and healthy. Conversely, there are many excellent studies of the effects of parenteral anesthetics in rodent models.

Drug Administration

Injection routes include subcutaneous (SC), intramuscular (IM), intraperitoneal (IP), intravenous (IV), and intraosseous (IO). Potentially irritant solutions (e.g., high or low pH solutions) should not be administered SC or IM, because of the risk of self-mutilation (Leash et al., 1973; Gaertner et al., 1987). Diluting the solution, avoiding large volume injections, and injecting in the proximal muscles of the legs reduce the risk of

Table 60.3. Parenteral anesthetic regimens and dosages (mg/kg) for representative rodents.

Species	Ketamine/ Acepromazine	Ketamine/ Xylazine	Ketamine/ Medetomidine	Ketamine/ Midazolam	Tiletamine/ Zolazepam	Propofol
Mouse	50-150/2.5-5.0 IP	50-200/5-10 IP		40-150/3-5 IP	50-80 IP	NA
Hamster	50-150/2.5-5.0 IP	50-150/5-10 IP		50-150/5 IP	50-80 IP	NA
Gerbil	NA	50-70/2-3 IP		40-150/3-5 IP	50-80 IP	NA
Rat	50-150/2.5-5.0 IP IV	40-90/5 IP		40-100/3-5 IP IV	50-80 IP IV	10 IV
Guinea pig, Chinchilla	20-50/0.5-1.0 IP IV	20-40/3-5 IP IV	5/0.06 IM (Henke et. al., 2004)	20-50/3-5 IP IV	20-40 IP IV	10 IV
Beaver, Capybara, Porcupine		5-10/1-2 IM	3-4/0.03-0.04 IM IV		4–6 IM IV	6-8 IV

Adapted, in part, from Flecknell PA. Anaesthesia and post–operative care of small mammals. *In Pract* 1991;13:180–189; Mason DE. Anesthesia, analgesia and sedation for small mammals. In: Hillyer EV, Quesenberry KE, eds. *Ferrets, Rabbits and Rodents. Clinical Medicine and Surgery*. Philadelphia: W.B. Saunders, 1997:378–391.

Use the lower dosages for debilitated animals and intravenous injection.

developing this adverse effect. Alternatively, drugs are administered by IP injection. Large rodents are enclosed in squeeze cages (Figure 60.2) or administered drugs using a remote injection system.

Vascular Access

Small size makes venous and intraosseous catheterization difficult, but practice and attention to technique enable attainment of these essential skills. Potential catheterization sites include the cephalic, saphenous, and auricular veins. The lateral coccygeal veins can be accessed in rats with small-gauge needles. Penetration of the skin before placement, with either a hypodermic needle or scalpel blade, is done to prevent catheter buckling. Intraosseous catheter sites include the proximal femur, tibia and humerus.

Parenteral Anesthetics

Some rodents (e.g., guinea pigs) have limb movement at ketamine or tiletamine/zolazepam dosages expected to produce surgical anesthesia. Ketamine (44 mg/kg) takes 8 to 10 mins for induction and has a very short duration of effect (15–20 minutes) (Weisbroth and Fudens, 1972). Ketamine and ketamine/xylazine may be associated with self-mutilation (Gaertner et al., 1987).

Xylazine and other α_2 -adrenergic agonists are frequently combined with ketamine for short-term immobilization and surgical anesthesia. These combinations, however, produce mild to severe dose-dependent hypotension, bradyarrhythmias, and respiratory depression (Hart et al., 1984; Wixson et al., 1987). Oxygen supplementation and assisted ventilation is recommended. Ketamine/benzodiazepine combinations produce less cardiopulmonary depression and analgesia, but good muscle relaxation.

In rats and mice acute reversible lens opacity has been observed with xylazine and xylazine/ketamine (Calderone et al., 1986). These "cataracts" were associated to a varying degree with proptosis, obtunded blink response, corneal surface drying, and mydriasis.

Although moderately effective for minor surgery in rats and gerbils, very high tiletamine/zolazepam dosages are required to prevent response to noxious stimuli in other species (i.e., mice, hamsters, and guinea pigs) (Silverman et al., 1983).

Propofol is used for induction and maintenance of anesthesia when administered as a continuous IV infusion or intermittent bolus. The propofol can be diluted with saline for injection in very small patients. Apnea is related to dose, rate of injection, and the presence of other drugs. The induction dose is dependent on rate of administration (Larsson, 1994). In rats, both fast (20 mg/kg per minute) and slow (2.5 mg/kg per minute) rates result in larger doses than those at an intermediate rate (10 mg/kg per minute). Propofol is a poor analgesic. It is indicated for induction of healthy rodents in which vascular access can be attained.

INHALATION ANESTHESIA

Inhalation anesthesia is the primary component of most, if not all, clinical anesthetic regimens.

Inhalant Anesthetics

Isoflurane is associated with rapid induction and recovery, and rapid control of anesthetic depth. It produces a dose-dependent cardiopulmonary depression, does not sensitize the myocardium to catecholamine-induced arrhythmias, and is a poor analgesic (Imai, 1999). Sevoflurane is similar to isoflurane, except it produces even more rapid induction and recovery.

Inhalant Induction

For induction inhalant anesthesia is used alone or as an adjunct to parenteral drugs. The anesthetic is administered into a chamber or through a mask. The advantage of an induction chamber is the animal is not manually restrained during the involuntary excitement phase of induction. This reduces injury to handler and patient. The disadvantages include greater potential for

environmental contamination with inhalation anesthetic and difficulty in monitoring.

Mask induction of manually restrained animals, without premedication and supplemental injectable anesthesia, is not recommended. Anesthetic chambers and masks are opaque to allow visualization of the patient. Chambers can be made from commercial plastic containers and sized to the animal (Figure 60.3). The chamber top should be able to be secured to prevent the animal forcibly opening it and escaping. For induction of an awake or lightly sedated animal, inhalant anesthetic is introduced into the container through one opening, and waste gas removed from another opening. The vaporizer is set at maximum concentration, and oxygen flow rate set at 2 to 4 L/minute depending on the size of the container. It takes a period of time for the concentration in the induction chamber to equilibrate with the vaporizer setting. The animal loses its righting response in 5 to 10 minutes and is removed from the chamber. A mask is placed over its nose and mouth, and the chamber is removed outside or closed to allow waste gases to be safely voided to the atmosphere. The animal is then either maintained using the mask or intubated when it is sufficiently relaxed.

When maintaining anesthesia with a mask, it is important to have the animal's head and neck in extension to facilitate air movement. Respiratory pattern, rate, and noise should also be assessed to ensure minimum resistance to breathing. If the animal appears to be having respiratory difficulty, move the head and neck to see whether the obstruction can be corrected. If not, use cotton-tipped applicators to clear the oropharynx and nares. If this fails to relieve the problem, intubate or wake the animal and cancel the procedure.

Equipment

Small size is an indication for a non-rebreathing system for administration of inhalant anesthetics. T-piece breathing systems are recommended for the smallest. Rebreathing bags can be constructed from small balloons to facilitate visualization of respiratory movement. Fresh gas flow rate for nonrebreathing systems is about 200 ml/kg per minute.

Inhalation anesthesia is often maintained with a mask connected to the breathing system. Systems have been developed for small rodents that also allow concurrent scavenging of waste anesthetic gases (Mauderly, 1975; Levy et al., 1980). These usually include the fresh gas line entering the mask and an exit line for removal of waste gases.

Endotracheal Intubation

Respiratory obstruction and hypoventilation are common limitations to diagnostic and surgical procedures. With practice and the use of appropriate technique and equipment, intubation should be a routine standard of care in some rodents.



Figure 60.3. Small to medium-sized rodents (e.g., agouti) can be induced with inhalant anesthetics administered into a chamber. These induction chambers can be made from commercially available plastic boxes that should be opaque and have a secure top.

Table 60.4. Guidelines for endotracheal tube size selection in rodents.

Species	Endotracheal Tube Internal Diameter (mm)
Rat	16–18 gauge over-the-needle catheter
Guinea pig, chinchilla	14–16 gauge over-the-needle catheter, ≤2
Hamster	16 gauge over-the-needle catheter
Eastern gray squirrel	≤2
Prairie dog	2.0-2.5
Capybara	6.0

There are a variety of commercially available endotracheal tubes; the smallest cuffed and uncuffed tubes have a 3- and 1-mm internal diameter (ID), respectively. Guidelines for endotracheal tube size are given in Table 60.4. Endotracheal tubes are preferably opaque for visualization of condensation or occlusion with mucous or blood. For the smallest patients endotracheal tubes are constructed from over-the-needle catheters or urinary catheters.

Guinea pigs present many obstacles to routine intubation. Their cheek pouches frequently contain stored food and they readily regurgitate if the oropharynx is stimulated. They produce profuse salivary secretions that can be controlled, in part, by glycopyrrolate. The soft tissue at the base of the tongue is readily traumatized by a laryngoscope blade resulting in profuse hemorrhage. The soft palate is fused to the base of the tongue, and entry to the glottis is through the small opening of the palatal ostium (Timm, 1987). The palatal ostium is also present in chinchillas and capybaras, and probably other hystericomorph rodents. The glottis is also very small relative to the size of the animal.

For these reasons, this author rarely intubates guinea pigs, but has had success using a blind technique. However, other authors describe intubation of dorsally recumbent animals using direct visualization techniques with modified pediatric #0 blades and 14-gauge over-the-needle catheters (Kujimi, 1981).

Rat intubation usually involves direct visualization of the glottis. It requires magnification and a focused light source (e.g., rigid endoscope). One technique describes transillumination with a high intensity light source in contact with the skin surface in front of the neck near the pharyngoepiglottic region (Yasaki, 1991). This author uses a rigid endoscope or an otoscope attached to a #2 ear speculum that has had the distal two-thirds of the tip along the right side removed (Tran, 1986). The rat is positioned in dorsal recumbency on a board. An elastic band is then affixed to the upper incisors and fastened to the board to extend the head and neck. The tongue is pulled forward and to the side and a cotton-tipped applicator is used to clear any secretions from around the glottis. Topical application of local anesthetic on the glottis reduces laryngospasm. A slight pressure exerted on the ventral surface of the neck may further facilitate visualization of the glottis. A blind technique, similar to that described above for other rodents, has also been reported (Stark, 1981).

Endotracheal tubes for rats are constructed from 14 to 16 g over-the-needle catheters. The needle stylette is cut to the same length as the catheter, and the end is then filed smooth so that the smoothed needle is approximately 1 mm shorter than the catheter (Stark, 1981). Alternatively, a 70-mm length of malleable 20-gauge wire is used as a stylet (Tran, 1986). At 1.5 cm from the end of the catheter, the stylette is bent at a 30-degree angle. A surgical suture can be tied to the catheter at a point 4.5 cm from its end to prevent excessive insertion of the catheter into the trachea. Mucous obstruction is common and changing the tube may be necessary. This technique can also be used for hamsters.

Prairie dogs, chinchillas, squirrels, and other medium to moderately large rodents (e.g., African pouched rats, maras) can routinely be intubated for inhalation anesthesia using a blind technique. The anesthetized rodent is laid in lateral recumbency, with the head and neck moderately extended. The tube is then passed in a similar manner to that described for the rabbit (see Chapter 59). Alternatively, an endotracheal tube can be placed with the assistance of an endoscope. The tube is placed over the scope or alongside it (Figures 60.4 and 60.5).

When in doubt remove the endotracheal tube and reassess placement. The use of a pulse oximeter is invaluable for determining potential oxygenation problems because of airway obstruction. Correct endotracheal tube placement is determined by: (1) visualizing condensation on either the inside of the endotracheal tube or a metal surface placed at the end of the tube; (2) detecting air movement with hair placed in front



Figure 60.4. For endotracheal intubation of chinchillas and other medium to large rodents, the glottis can be visualized with an endoscope.



Figure 60.5. Although they are large, capybara are difficult to intubate. In this anesthetized animal an endoscope is being placed directly into the glottis; the endotracheal tube is then slid off the endoscope.

of the tube; (3) watching the non-rebreathing bag; (4) the response to intubation (coughing, etc.); and (5) the detection of exhaled carbon dioxide on a capnograph. To ensure the tube has not been placed into a single bronchus, premeasure the tube before use, and auscultate both lung fields for respiratory sounds after intubation.

MONITORING

Monitoring is described in Chapter 6. It is recommended a trained person be assigned as anesthetist for each patient. This facilitates monitoring, recording, and supportive care, and saves time when intervention is required.

Unconsciousness is based on anesthetic dose and vaporizer setting, muscle relaxation, decreased reflex activity, and absence of limb and body movement. Palpebral and corneal reflexes are observed at 0.8 MAC, but are abolished at greater than 2.0 MAC (Imai, 1999). The corneal reflex, however, is a poor guide to anesthetic depth (Imai, 1999). A fixed dilated pupil, unresponsive to light is a cross-species indicator of excessive depth. Anal tone is retained until deep anesthetic levels, but is difficult to assess in small rodents.

Pain and nociceptor responses are assessed with a toe, ear, and tail pinch, or a skin incision. Increasing depth is assumed when muscle tone (e.g., jaw muscle, anal sphincter) decreases, palpebral and corneal reflexes are obtunded, and respiration pattern becomes regular and even. Sudden tachycardia, hypertension, or tachypnea in response to stimuli is indicative of inadequate anesthetic depth or analgesia.

Rodent heart rates are determined by temperature, size, metabolism, respiratory state, and the presence or absence of painful stimuli. Heart rate is inversely related to body size. The resting heart rate for mammals is calculated from the allometric equation $241 \times M_b^{-0.25}$, where $M_b = \text{body weight (kg) (Schmidt-Nielsen, 1984)}$. A heart rate 20% above or below the calculated rate for an individual is considered either tachycardic or bradycardic, respectively.

The esophageal stethoscope is not practical to use in small rodents and it may induce regurgitation in guinea pigs. Alternatively, a quality pediatric stethoscope is used. The electrocardiograph should have a multichannel oscilloscope with non-fade tracing and freeze capabilities. Additionally, it must be able to record at speeds of 100 mm/second and amplify the signal to at least 1 mV equal to 1 cm. Standard lead positions are used.

The Doppler flow detector is used anywhere there are major arteries close to the skin. These include the ventral aspect of the tail base, the carotid, femoral and auricular arteries, and directly over the heart. Potential sites for indirect blood pressure measurement include the legs, forearms, tail, and ears. Indirect blood pressure measurement techniques have been designed and validated for use in rats (e.g., Widdop and Li, 1997; Ibrahim et al., 2006).

As with cardiac auscultation, evaluation of the respiratory system requires a good-quality stethoscope with appropriate head and length of tubing, and an experienced ear. Pulse oximetry has been evaluated in rats, and appears accurate at hemoglobin saturation levels greater than 70% (Decker et al., 1989). Potential sites for placement of transmission pulse oximeter sensors include the ear, tongue, buccal mucosa, paw, vulva, prepuce, and proximal tail (Decker et al., 1989). A reflectance pulse oximeter sensor is used in either the esophagus or the rectum or applied to the skin/fur surface on the ventral aspect of neck overlying the carotid artery (rat).



Figure 60.6. An anesthetized fox squirrel. The animal was intubated with an uncuffed 2 mm ID tube using a blind technique. A capnograph is used to assess correct placement. A 24-g over-theneedle has been placed in the cephalic vein for fluid administration.

Hypothermia is common in anesthetized rodents because of the large surface area to volume ratio. Additionally, many anesthetics suppress normal thermoregulatory mechanisms. Further, anesthetic gases are of low humidity and temperature. Body temperature is preferably measured continuously and the thermometer should be sufficiently small to be used in small patients. For measurement of core body temperature, it is necessary to use a temperature probe attached to an esophageal stethoscope.

SUPPORTIVE CARE

Vascular access is discussed in the preceding. The cephalic vein is able to be catheterized in medium to large rodents (Figure 60.6). Small volume infusers are essential for accurate fluid infusion in small patients. Some can be preprogrammed to flow rates for emergency and other drugs, so that all that is necessary for administration is to enter the body weight of the animal. They also allow a continuous infusion, which is preferable to bolus injection.

General anesthetics usually produce a dosedependent ventilatory depression. This effect may be either additive or synergistic with underlying disease resulting in marked hypercapnia and/or ventilatory arrest. High-inspired oxygen concentrations also decrease ventilatory drive. Ventilation is also affected by body position and compression of the respiratory exchange tissues by distended viscera and/or obesity. Inadvertent compression of the chest by surgeons is common in small exotic patients. Developing good hand position techniques, an attentive anesthetist, and the use of clear plastic drapes helps prevent this cause of hypoventilation. Guinea pigs have relatively small diameter tracheas, and are prone to airway obstruction because of regurgitation and profuse salivary secretions. Adequacy of ventilation is most accurately assessed using PaCO₂. Capnography provides an indirect estimate of PaCO₂, but is too inaccurate in most small exotic patients to be used for anything other than validation of successful endotracheal intubation. Visualization of chest wall movement is a deceptive guide to adequacy of ventilation. Consequently, the author recommends either assisted or controlled ventilation of intubated patients under general anesthesia. Doxapram is not recommended for use in hypoventilating patients unless intubation and mechanical ventilation is impossible or contraindicated.

Ventilation is either assisted or controlled by positive pressure either manually or mechanically. Many of the ventilators used in small animal anesthesia can be modified to ventilate rodents. A commercially available combination ventilator and anesthesia machine (Anesthesia WorkStation, Halowell EMC, Pittsfield, MA) has been designed for research rodents. It is both a circle system for delivery of inhalant anesthetic and an optional ventilator with an adjustable pressure safety limit. The advantage of mechanical ventilation is that it frees the anesthetist to concentrate on other tasks. The disadvantages are that mechanical ventilators require a thorough theoretical and technical understanding for their safe use, they require endotracheal intubation, and they produce positive intrathoracic pressures that interfere with venous return to the heart and may cause lung trauma.

Manual ventilation provides the advantage, with a skilled anesthetist, of rapidly adjusting ventilatory pressures and volumes, and responsiveness to the surgeon who may require brief irregular periods of ventilatory arrest to safely complete a procedure. Further research is necessary to evaluate the efficacy and appropriateness of ventilation techniques in small mammal practice. There may be situations in which some hypoventilation is preferable to the adverse effects of positive pressure ventilation.

Administration of elevated inspired oxygen concentrations (greater than 40%) often overcome mild to moderate hypoxemia, assuming no major pulmonary shunting is present. Although mammals are susceptible to pulmonary oxygen toxicity, this syndrome is unlikely to be observed in patients maintained on high-inspired oxygen concentrations for 24 hours.

Minimizing anesthesia time and the use of warm surgical preparation solutions, wrapping the body, increasing the room temperature, and using external heat sources (i.e., circulating warm water blankets and forced-air warmers) reduces hypothermia. Electric heat blankets are not used because they have the potential to cause severe burns. Similarly, heated fluid bags placed in contact with the skin may cause burns. If endotracheal

intubation is not possible, an indirect ventilation technique using a bulb inflator placed over the nose can be used in small rodents (Ingall and Hasenpusch, 1966).

RECOVERY

The patient is placed in a warm, quiet environment and monitored. Supportive care is continued until the patient is fully alert and physiologically stable. Vascular access is maintained to allow emergency administration of drugs and fluids. Drugs, procedure duration and the magnitude of physiological dysfunction incurred determine duration and quality of recovery. Prolonged recovery is usually owing to hypothermia, hypoglycemia, and anesthetic overdose and/or impaired drug elimination. Rewarming exacerbates underlying hypovolemia and hypoglycemia.

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Editors:

Gary West is the Director of Veterinary Services at the Oklahoma City Zoo and an Adjunct Assistant Professor at Oklahoma State University.

Darryl Heard is an Associate Professor and Service Chief of Zoological Medicine at the College of Veterinary Medicine, University of Florida.

Nigel Caulkett is a Professor of Anesthesiology in the faculty of Veterinary Medicine, University of Calgary.

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